

MEDICAL PROCEEDINGS

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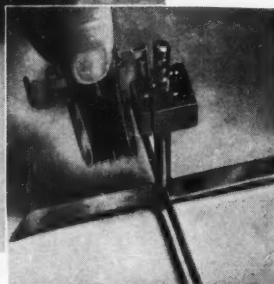
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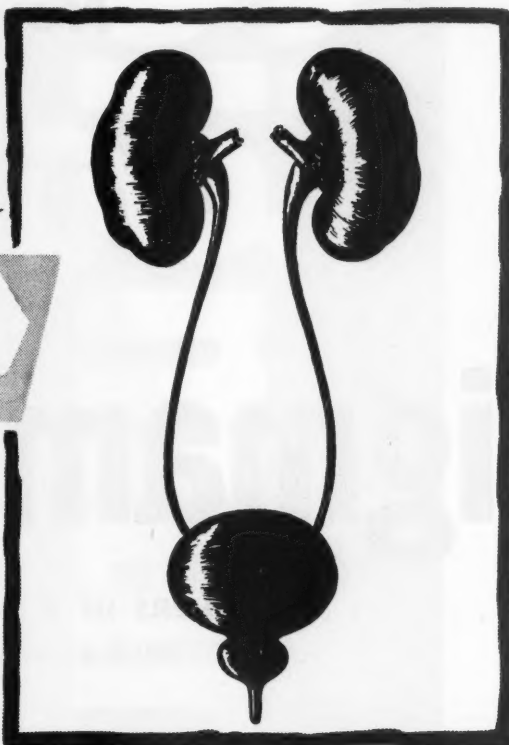
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Ref. SOBIN et al Antibiotics Annual 1954-55
p. 827.

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Ref. Personal communication presented
at Antibiotic Symposium 1956.

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Ref. ENGLISH et al Antibiotics and Chemo-
therapy VI: 511. Aug. 1956.

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Ref. Royes et al Antibiotics and Chemo-
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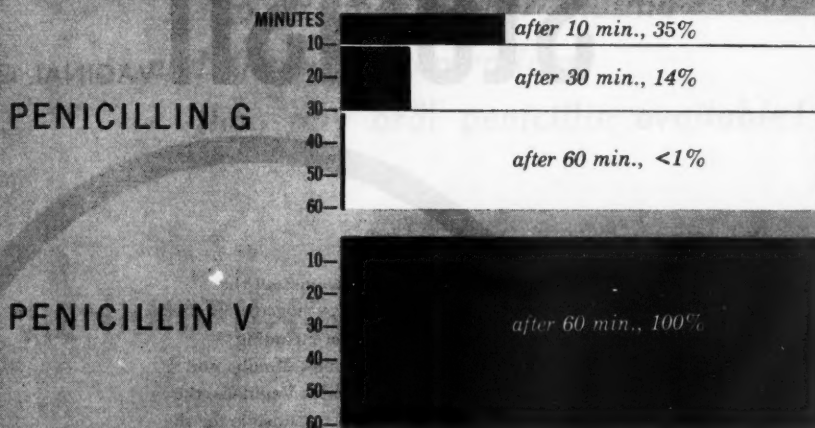
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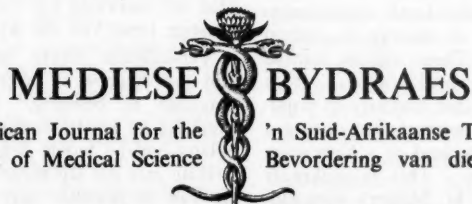
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EDITORIAL · REDAKSIONEEL

DISCOGRAPHY IN THE DIAGNOSIS OF INTERVERTEBRAL DISC LESIONS IN THE LUMBAR REGION

A SOUTH AFRICAN CONTRIBUTION

The modern concept of lumbar disc lesions really only dates from 1934 when Mixter and Barr¹ presented an historic communication on the subject. Kocher² in 1896 appears to have been the first to describe an actual posterior displacement of intervertebral disc material in a man who had fallen 100 feet to land in a standing position.

Since Mixter and Barr's communication our knowledge of intervertebral disc lesions has progressed very rapidly. Lesions of the intervertebral discs in the lower lumbar region have come to be recognized as the most important cause of low backache and/or sciatica. Indeed, according to Albert Key,³ almost all cases of low back pain with or without sciatica are due to lesions of the intervertebral discs in the lumbo-sacral region.

While the clinical diagnosis in many cases is comparatively simple, its pre-operative verification is by no means so. The plain X-ray of the spinal column may show signs which

DISCOGRAFIE BY DIE DIAGNOSE VAN TUSSENWERWELSKYFLETSELS IN DIE LENDESTREEK

'N SUID AFRIKAANSE BYDRAE

Die huidige opvatting van letsels van die lendetussenwerwelskywe dagteken in werklikheid slegs uit die jaar 1934 toe Mixter en Barr¹ 'n historiese referaat oor die onderwerp gelewer het. Dit skyn asof Kocher² in 1896 die eerste was wat agterwaartse verplasing van 'n tussenwerwelskyf beskryf het by 'n man wat 100 voet geval het en op sy voete te lande gekom het.

Sedert Mixter en Barr se mededeling het ons kennis van letsels van die tussenwerwelskywe vinnig toegeneem. Daar word vandag erken dat letsels van die tussenwerwelskywe in die laer lendestreek een van die vernaamste oorsake van lae rugpyн en/of heupjig is. Trouens, volgens Albert Key³ moet byna alle gevalle van lae rugpyн (met of sonder heupjig) toegeskryf word aan letsels van die tussenwerwelskywe in die lende-heiligbeen-streek.

Terwyl die kliniese diagnose in baie gevalle betreklik eenvoudig is, is die voor-operasie-bevestiging daarvan geensins so maklik nie.

1. Mixter, W. J. and Barr, J. S. (1934): New Eng. J. Med., **211**, 210.
2. Kocher, T. (1896): Mitt. s.d. Grenz geb. d. Med. u. Chir., **1**, 420.
3. Key, J. Albert (1949): The American Academy of Orthopaedic Surgeons: Instructional Course Lectures, **10**, 27. Ann Arbor, Michigan: J. W. Edwards.

1. Mixter, W. J. en Barr, J. S. (1934): New Eng. J. Med., **211**, 210.
2. Kocher, T. (1896): Mitt. s.d. Grenz geb. d. Med. u. Chir., **1**, 420.
3. Key, J. Albert (1949): The American Academy of Orthopaedic Surgeons: Instructional Course Lectures, **10**, 27. Ann Arbor, Michigan: J. W. Edwards.

may indicate a disc lesion, but often these signs are completely absent, even in the presence of a gross disc lesion.

Various types of specialized examination have been employed in an attempt to confirm the clinical diagnosis. These include lumbar puncture and contrast myelography. It is important to emphasize that, contrary to popular belief, puncturing a normal disc during a lumbar puncture will not lead to a herniation of the nucleus pulposus. This is strikingly demonstrated by Mr. L. H. Muller's outstanding contribution published elsewhere in this issue, an investigation undertaken under the guidance and stimulus of Mr. Johan du Toit, Head of the Orthopaedic Department at the Pretoria General Hospital and Senior Lecturer in Orthopaedics at the University of Pretoria Medical School.

Contrast myelography has gained a varying degree of popularity in different centres. It is readily admitted that it has a place in the diagnosis of the pathology in cases of low back pain. It is indispensable in the diagnosis of conditions like cauda equina tumours, and arachnoiditis. In the diagnosis of disc lesions, however, it can only be positive in cases of disc herniation and not in the equally important cases of disc degeneration, where it is always negative. In cases of herniation or prolapse of the nucleus pulposus, contrast myelography is of definite value. It is, however, only positive in about 70% of cases. In about 30% of cases it gives an inaccurate result which may be either falsely positive or falsely negative.⁴ The limitations of contrast myelography are thus patent.

Direct visualization of the intervertebral disc by discography would appear to be a more accurate method of demonstrating the condition of the disc itself. This investigation was initiated by Erlacher⁵ in 1949 and subsequently taken a step further by Knut Lindblom.⁶ The technique of discography is described in this issue by Mr. Muller, who punctures the 4th and 5th lumbar intervertebral discs transdurally by means of thin lumbar puncture needles under radiographic control. This has to be carried out with a degree of asepsis comparable with that used in the operating theatre. With experience the tech-

'n Gewone X-straal-plaat van die werwelkolom toon miskien tekens wat dui op 'n individuele skyfletsel, maar dikwels is hierdie soort tekens glad nie aanwesig nie—selfs in gevalle van 'n ernstige letsel van die skyf.

Verskillende soorte spesiale ondersoeke is dan ook toegepas in 'n poging om die kliniese diagnose te bevestig. Hulle sluit lumbale punkties en kontrasmielografie in. Dit is van belang om die feit te beklemtoon dat, in teenstelling met die algemene opvatting, die punksie van 'n normale skyf in die loop van 'n lumbale punksie nie aanleiding gee tot herniasie in die skyfkern nie. Dit word op 'n opvallende manier gedemonstreer deur mnr. L. H. Muller in sy voortrefflike bydrae wat elders in hierdie uitgawe verskyn. Die ondersoek is onderneem onder die leiding en op aandrang van mnr. Johan du Toit, hoof van die Ortopediese Afdeling aan die Algemene Hospitaal in Pretoria en Senior Lektor in Ortopedie aan die Mediese Skool van die Universiteit van Pretoria.

Kontrasmielografie word meer gebruik in sommige sentrums as in ander. Daar word gereedelik toegegee dat dit 'n plek verdien in die diagnose van die patologie van gevalle van lae rugpyn. Dit is onontbeerlik by die diagnose van toestande soos cauda equina-gewasse en arachnoiditis. By die diagnose van skyfletsels kan dit egter positief wees slegs in gevalle van skyfuitsteking en nie in die ewe belangrike gevalle van skyfdegenerasie nie. In gevalle van herniasie of uitsteking van die skyfkern is kontrasmielografie van definitiewe waarde. Slegs in 70% van al die gevalle is dit egter positief. In ongeveer 30% van die gevalle lewer dit 'n onjuiste resultaat op wat of foutief positief of foutief negatief kan wees.⁴ Die beperkings van kontrasmielografie lê dus voor die hand.

Regstreekse betragting van die tussenwerwelskyf deur middel van discografie skyn dus 'n noukeuriger metode te wees om die toestand van die skyf self te demonstreer. Hierdie ondersoek is in 1949 deur Erlacher⁵ van stapel gestuur en later 'n stap verder gevoer deur Knut Lindblom. Die tegniek van discografie word in hierdie uitgawe beskryf deur mnr. Muller wat die 4de en 5de lumbale tussenwerwelskywe transduraal binnegedring het mer

4. Wolkin, J., Sachs, M. D. and Hoke, G. H. (1955): *Radiol.*, **64**, 704.

5. Erlacher, P. R. (1952): *J. Bone Jt. Surg.*, **34-B**, 204.

6. Lindblom, K. (1954): *Quoted by Friberg, S.* (1954): *Bull. Hosp. Jt. Dis.*, **15**, 1.

4. Wolkin, J., Sachs, M. D. en Hoke, G. H. (1955): *Radiol.*, **64**, 704.

5. Erlacher, P. R. (1952): *J. Bone Jt. Surg.*, **34-B**, 204.

6. Lindblom, K. (1954): *Aangehaal deur Friberg, S.* (1954): *Bull. Hosp. Jt. Dis.*, **15**, 1.

nique can be improved and simplified. In most cases the patient experiences no greater discomfort than with a lumbar puncture. Pyelosil, a 50% water-soluble iodine compound, is used for injection into the disc.

Discography gives an accurate result in 92% of cases.⁴ It is impossible to obtain a false negative result with discography; there may be false positive results, but this is usually due to faulty interpretation and should be minimized with increased experience.

Only a few series of investigations by discography have been published up to the present time. The contribution from Pretoria is thus of the greatest importance from the diagnostic and technical points of view.

Discograms have been performed in 75 cases at the Pretoria Hospital Orthopaedic Department. This series is sufficiently large to justify certain conclusions and lends support to the view amongst workers who have experience of both contrast myelography and discography, that the latter procedure is very definitely superior.

Discography indicates the presence and the exact degree of degeneration of the disc. There are no false-negative discograms. Where the disc is found to be normal it can be ruled out as the cause of the signs and symptoms. A negative myelogram, by contrast, does not indicate the absence of degenerative changes in the disc, which may still be the cause of the symptoms. Discography also shows up the presence of any herniation of the nucleus pulposus and its exact location. A contrast myelogram frequently shows up a herniation or prolapse, but if the retropulsion is laterally placed it does not impinge on or deform the column of the contrast medium and hence a negative myelogram does not rule out a disc herniation. False positive myelograms are not uncommon and may lead to confusion.

While contrast myelography has a very definite place in the diagnosis of suspected intradural and some cases of extradural pathology of disc lesions in the lumbar area, discography may well prove to be superior. It is a direct, safe and accurate method of investigation of the intervertebral disc.

There would appear to be a very real justification for investigating a series of cases by both contrast myelography and discography in order to assess the relative merits and demerits of each procedure. The researches from the University of Pretoria have given a striking lead in this field.

behulp van dun lumbale punksienaalde onder radiografiese beheer. Dit moet gedoen word met 'n mate van asepsis wat vergelykbaar is met dié wat in die operasiesaal toegepas word. Met ondervinding kan die tegniek verbeter en vereenvoudig word. In die meeste gevalle ondervind die pasiënt geen groter ongerief as dié wat uit 'n lumbale punksie voortspruit nie. Pyelosil, 'n jodiumsamestelling wat in water oplosbaar is, word as 'n 50% oplossing gebruik vir inspuiting in die skyf.

Discografie gee 'n akkurate resultaat in 92% gevalle.⁴ Dit is onmoontlik om 'n foutief negatiewe resultaat met discografie te verkry. Daar kan foutief positiewe resultate wees, maar dit moet gewoonlik toegeskryf word aan 'n foutiewe vertolking, en, met groter ondervinding, behoort dit uit die weg geruim te kan word.

Verslae oor slegs 'n paar reekse discografiese ondersoeke is tot dusver gepubliseer. Die bydrae van Pretoria is dus uit 'n diagnostiese en tegniese standpunt van die allergrootste belang.

In die Ortopediese Afdeling van die Pretoriase Hospitaal is discogramme in 75 gevalle gedoen. Hierdie reeks is groot genoeg om sekere gevolgtrekkings te regverdig, en steun die standpunt van werkers met ondervinding van sowel kontrasmielografie as discografie dat laasgenoemde prosedure definitief beter is.

Discografie dui die aanwesigheid en die presiese mate van degenerasie van die skyf aan. Daar is geen foutief negatiewe discogramme nie. In gevalle waar daar bevind word dat die skyf normaal is, kan dit uitgeskakel word as die oorsaak van die tekens en simptome. In teenstelling daarmee dui 'n negatiewe mielogram nie die afwesigheid van degenerasieveranderinge in die skyf aan nie—iets wat nog altyd die oorsaak van die simptome kan wees. Discografie toon ook aan of daar enige uitsteking van die skyfkern is, en, indien wel, presies waar dit geleë is. 'n Kontrasmielogram toon dikwels uitsteking aan, maar as die uitsteking lateraal geleë is, bots dit nie teen of vervorm dit nie die kolom van die kontrasmiddel nie. Gevolglik sluit 'n negatiewe mielogram nie die moontlikheid van uitsteking van die skyfkern uit nie. Foutief positiewe mielogramme is geen ongewone verskynsel nie, en kan aanleiding tot verwarring gee.

Kontrasmielografie het 'n baie definitiewe plek in die diagnose van verdagte binnedekvliesige en ook in sommige gevalle van buitedekvliesige patologie, hoewel discografie bes moontlik die bewys kan lewer dat dit doeltreffender is in die diagnose van skyfletsels in die lumbale streek. Dit is 'n regstreekse, veilige en akkurate metode om die tussenwerwelskyf te ondersoek.

Dit skyn asof daar goeie regverdiging is vir die ondersoek van 'n reeks gevalle deur sowel kontrasmielografie as discografie sodat die betreklike voor- en nadele van albei prosedures vasgestel kan word. Die navorsingswerk wat by die Universiteit van Pretoria gedoen is, het opvallend goeie leiding op hierdie gebied gegee.

PENICILLIN REACTIONS

THEIR PREVENTION BY HIGH DOSAGE OF PARENTERAL ANTIHISTAMINES

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Since 1949, when Waldbott¹ reported the first case of death due to penicillin, the frequency of reports of penicillin reactions, of varying severity, has become disturbing, the more so when it is apparent that there are many unreported cases of fatal and near-fatal reactions. In the past few years penicillin has headed the list of all drugs in its frequency of production of sensitivities, and far surpasses the sera in its production of anaphylactic reactions.² Yet it is still being produced at the rate of 400 tons per year.³

Reports in the literature are most confusing on all aspects of penicillin reactions and sensitivity, the statistics varying between 1-53% for all penicillin reactions, while Welch in 1953 estimated that 30% of all anaphylactic reactions in the United States of America were fatal.

In 1951, it was reported that penicillin by mouth causes few or no disagreeable side effects, but the fallacy of this statement is well illustrated in the recent literature. In the past year, 3 cases of anaphylaxis from penicillin were experienced and reported by one worker,⁴ while others reported that, although they were able to find a report of one case of death in a child from penicillin, nevertheless they personally had knowledge of 2 unrecorded cases of death in children due to penicillin.⁵ The use of penicillin ointment in the eye has resulted in an immediate anaphylactic reaction,⁶ as did the use of penicillin for scratch-testing in a dilution of 10 units per c.c.⁷

The potency of penicillin antigenicity is demonstrated in the very interesting studies of Coleman and Siegel,⁸ who have shown that once a syringe has been used for administering penicillin, ordinary methods of syringe sterilization are ineffective in destroying the antigenic power of this antibiotic: and they doubt whether the new high-pressure method of sterilization designed to prevent the spread of hepatitis will be sufficient to prevent this hypersensitizing faculty imparted to such penicillin-contaminated syringes. It has also been shown that epidermophytosis is antigenically related to penicillin.⁹

It is stressed by many workers that, before penicillin therapy in a patient, a detailed personal history should be obtained of untoward previous reactions to penicillin; also a detailed personal and family history of allergy. The assumption that one can use penicillin in a patient who denies any previous reaction with penicillin is contrary to the basic principles of allergy, anaphylaxis occurring in those who previously have had sensitizing exposure to the drug.¹⁰ In their series of cases, Matthews *et al.*¹¹ found there was a slight trend towards a higher incidence of allergic rhinitis, asthma and urticaria amongst the reactor group than among the non-reactors, but this difference was not significant and the trend regarding family history of allergy was in the opposite direction. Previous use of penicillin ointment was noted more than twice as often in the reactor group, although the number of cases was not statistically significant. They also noted that a greater percentage of penicillin reactors complained of moderate to severe local reactions at the injection site.

The reason for the great variation in the reaction rates reported in the literature^{11, 15-22} is that more than 50 types of alleged penicillin reactions have been described, although all of these are not allergic in type; and unfortunately there is no reliable test for proving the diagnosis of all types of penicillin allergy. Patch testing has proved relatively reliable in the occasional case of penicillin contact dermatitis. Intracutaneous tests were abandoned in favour of scratch tests⁴ (one death being reported following an intracutaneous test for penicillin sensitivity). But even with scratch testing, the results are unsatisfactory. Minimal quantities of allergin must be used, and there is at present a strong consensus of opinion that scratch testing is unreliable in evaluating the vast majority of penicillin reactions, or predicting delayed reactions to penicillin, since this type of reaction has been seen in cases with negative skin tests.¹⁰ It is not known for how long positive skin tests persist after anaphylaxis to penicillin or for how long the capacity to develop anaphylaxis persists after

the initial penicillin anaphylactic reaction.¹² Penicillin allergy is often spontaneously lost over a variable period of time. At best, it is hoped, but not proved, that a negative skin test indicates the unlikelihood that anaphylaxis will develop. Passive transfer tests have been done,¹³ but these only indicate via an independent subject whether the serum of the patient still shows antigenic sensitivity to penicillin, and there are many drawbacks to this test. In the course of studies entailing passive transfer testing,³ one of the prior subjects was used as transfer site, and it was found that distinct whealing reaction was produced by injecting a vaccine diluted 1:25, the vaccine literature stating that it contained 'not over 100 units of penicillin per c.c.' One must conclude that as long as penicillin is used in the preparation of any vaccine, the administration of such vaccine can be expected to produce some allergic phenomena, particularly if used in groups older than infants and young children.

In practice to-day, as I have myself experienced before adding an antihistamine to penicillin injections, local and general reactions to penicillin are not uncommon. Moreover, acute anaphylactic reaction to penicillin of a fatal or near-fatal nature is far too frequent an occurrence. In one of my cases, which occurred before the series of cases described later, the patient, after an injection of penicillin, complained that he felt light-headed, giddy, nauseous and almost fainted. On the following day, the same patient was given another injection of penicillin and he manifested all the symptoms of an anaphylactic reaction.

The early symptoms of anaphylaxis following penicillin administration are a sensation of pins and needles in the body, a strong penicillin taste in the mouth, and vomiting, and a sensation of choking clinically presenting as asthma with marked cyanosis, rapidly followed by peripheral vascular collapse and loss of consciousness. In cases of anaphylaxis following penicillin, most active treatment embracing tying a tourniquet above the injection site, injections of adrenaline into the former injection site and also intramuscularly, injections of antihistamines and steroids and resuscitative measures, are urgently instituted to prevent a fatality. However, the prevention of death following penicillin anaphylaxis cannot be directly attributed to the counter-effect of any one drug used.

Among the methods suggested for decreasing the incidence of penicillin reactions,¹³⁻²² the prophylactic administration of antihist-

amines appears logical, especially as these drugs do not appear to affect the therapeutic efficacy of the penicillin; and solutions of antihistamines can be added to penicillin as diluents, which ensure that the patient receives the drug with no added inconvenience.

Again, one finds very conflicting results published in the literature where antihistamines have been used in an attempt to decrease the incidence of penicillin reactions, the confusion possibly being due to the fact that antihistamines were used by workers in different concentrations. Matthews *et al.*¹¹ concluded that an oral and/or parenteral antihistamine failed to produce any significant effect on the incidence of delayed or severe penicillin reactions, although there was a reduction of early reactions, particularly those of an urticarial type. Nevertheless, Maslansky and Sanger²⁶ in their series of cases found that, of 897 unselected patients given one, two or more injections of penicillin, only one showed a delayed reaction of an urticarial type; while in another series of 11 known penicillin-sensitive cases, only two patients had reactions following penicillin administration combined with an antihistamine; and in the latter series of 11 patients, the two reactors found their symptoms (in one case a rash and in the other case, anal pruritus) easily controlled with antihistamines. In Maslansky and Sanger's series of 897 cases, each injection of penicillin had admixed with it 10 mg. of chlorphenpyridamine (Chlor-Trimeton, Schering Corporation), while in the series of 11 known penicillin-sensitive cases each injection of penicillin was admixed with 20 mg. of Chlor-Trimeton (Schering Corporation).

In October 1955, having experienced the near-fatal case of anaphylactic reaction due to penicillin earlier described in this article, I decided to use antihistamines routinely with the parenteral administration of penicillin in the same dosage as that used by Maslansky and Sanger for their series of 11 penicillin-sensitive cases (viz. 20 mg. of antihistamine per injection), with the reservation that, if any untoward side effects of the antihistamine were noticed, the dosage of antihistamine would be decreased. The antihistamine selected for routine use was chlorphenpyridamine (Chlor-Trimeton, Schering Corporation) in the concentration of 100 mg. per c.c. and Crysticillin Aqueous Suspension (Squibb) 300,000 units per c.c. was used throughout. It was decided not to use the so-called hypo-allergic penicillins as they have been equally guilty of causing

side reactions.¹⁷ Using a sterile technique, 1.0 c.c. of Chlor-Trimeton injection 100 mg. per c.c. was injected into a vial containing 10 c.c. of Crysticillin Aqueous Suspension 300,000 units per c.c., the bottle of Crysticillin then being suitably marked with a plus sign to indicate the addition of Chlor-Trimeton to the Crysticillin; and before use, the vial was well shaken. The minimum quantity of Crysticillin-Chlor-Trimeton mixture used for injection was 2.2 c.c., which means that each patient received 600,000 units of Crysticillin and 20 mg. of Chlor-Trimeton, irrespective of the age of the patient (child or adult); and in a few cases, e.g. where infection was heavy, up to 5.5 c.c. of Crysticillin-Chlor-Trimeton mixture was given per injection.

During the course of the past 15 months, over 1,000 injections of Crysticillin-Chlor-Trimeton were given by me to 632 unselected patients, of whom one had, within one month before receiving these injections, had a course of penicillin injections without any added antihistamine, and with the last injection of that course had exhibited symptoms similar to those experienced by the patient described above before his penicillin anaphylaxis. However, this penicillin-sensitive case had no untoward reactions whatever while having Crysticillin with added Chlor-Trimeton, nor did he have any delayed reactions.

The dosage of Chlor-Trimeton per injection was not decreased, because in this entire series of cases, only one patient complained of drowsiness after 2.2 c.c. of the Crysticillin-Chlor-Trimeton mixture, and the duration of the drowsiness was about 2 hours.

The incidence of anaphylactic reactions in this series was nil, nor were any general reactions noted, only two cases exhibiting allergic manifestations. In both cases a large, red, indurated wheal occurred at the injection site, accompanied by itchiness, but all these symptoms disappeared within 48 hours.

DISCUSSION

One finds many conflicting reports in the literature on the results of parenteral antihistamine administration in the prophylaxis of penicillin reactions^{17, 20, 22, 23, 26} in both unselected and known penicillin-sensitive cases. In most of the reported series of cases the amount of antihistamine used varied from 3-20 mg. per dose, the latter high dosage of antihistamine (20 mg. of Chlor-Trimeton per injection) being used in only one series of cases²⁶ consisting of 11 known penicillin-sensitive

cases, of whom only 2 had a mild reaction following the parenteral administration of penicillin admixed with the high dosage of Chlor-Trimeton.

In the series of cases reported in this article, it was decided to use a high dosage of antihistamine parenterally (20 mg. Chlor-Trimeton Schering Corporation per injection), and this high dosage of Chlor-Trimeton was maintained throughout the entire series of over 1,000 injections of penicillin given, as only one case in my series (0.16%) reported a side effect attributable to the high dosage of Chlor-Trimeton (drowsiness), and that side effect was not of a severe nature. The incidence of allergic reaction in this series of over 1,000 injections of Crysticillin with 20 mg. of Chlor-Trimeton was 0.32% (representing 2 cases), which compares most favourably with the reports of other workers. In both these cases the reaction was of a mild nature at the site of the injection. One case with a history suggestive of penicillin sensitivity showed no reaction whatever.

The routine use of an antihistamine has been strongly recommended in cases requiring desensitization to certain allergens, where it has been found that the desensitizing allergen can be given in increasing and also in far higher dosage if used with a 'cover' of antihistamine.²⁷ In one case suffering from severe hay fever, who developed an angio-neurotic reaction when scratch-tested against the common inhalant allergens, and who developed the same reaction when given an intradermal injection of 0.1 c.c. of vaccine containing these allergens in a dilution of 20 units per c.c., it was decided to give an antihistamine subcutaneously with each desensitizing dose of allergen, Chlor-Trimeton being used in a dosage of 5 mg. for each different allergen in the vaccine. In this case 20 mg. of Chlor-Trimeton were given subcutaneously at the time of each injection. The desensitizing allergen was, of course, given intradermally.

CONCLUSIONS

The prevention of penicillin reactions of all severities, as well as reactions to various other injections (mainly protein injections, e.g. allergens) is vitally important.

In the light of the results published by other workers, as well as the results of the series of cases quoted in this article, an antihistamine in high dosage admixed with the injection appears to be adequate in controlling allergic reactions manifested after injections, particularly of penicillin. Such reactions are being

seen all too frequently.

A high dosage of antihistamine admixed with penicillin does not cause any side effects of an incapacitating nature. It reduces the incidence of allergic reactions to penicillin almost to zero and may, on occasion, be life-saving.²⁸

OPSOMMING

Die voorkoming van ernstige en minder ernstige penisillien-reaksies, sowel as die reaksies op verskillende ander inspuitings (hoofsaaklik proteïeninspuitings, bv. allergeene) is van die allergrootste belang.

In die lig van die resultate wat deur ander navorsers behaal is, sowel as die resultate van die reeks gevalle wat in hierdie artikel aangehaal word, skyn dit asof 'n groot dosis antihistamien, gemeng met die inspuiting, doeltreffend is vir die beheer van die allergiese reaksies wat hul verskyning na inspuitings—veral van penisillien—maak. Hierdie soort reaksies word glad te dikwels waargeneem.

'n Groot dosis antihistamien gemeng met penisillien het geen onbekwaammakende bykomstige effekte nie. Dit verminder die voorkoms van allergiese reaksies op penisillien feitlik tot nul, en kan in bepaalde gevalle die lewe van 'n pasiënt red.

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A MEDICAL ATLAS

TETANUS NEONATORUM

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Fig. 1 shows a child in severe opisthotonus. It is a case of tetanus neonatorum, a disease caused by *Clostridium tetani*. This is an anaerobic spore-forming organism which is widely distributed in soil, especially in rural areas. Like diphtheria, the infection remains localized, the symptoms being produced by a highly lethal toxin.

Since the introduction of active immunization the incidence of tetanus has greatly decreased. In rural areas, especially amongst Africans where the mother is delivered on the floor (which is commonly polished with animal dung) and often with only an untrained person

in attendance, there is still quite a high incidence of tetanus neonatorum. In the Coronation Hospital during the past 5 years there have been 21 cases, of which only 4 have survived, a mortality rate of approximately 80%. All these cases were confined outside the Johannesburg Municipal area. In no case was a qualified midwife in attendance. The instruments for severing the cord were usually cutting instruments in daily domestic use. Among certain sections it is customary to apply a mixture of soil and dung to the cut umbilical cord.



(Photograph by Dr. A. D. Benisau).

Fig. 1. Tetanus neonatorum.

The incubation period is 5-14 days, but may be prolonged for several weeks. The usual presenting symptom is difficulty in sucking due to trismus of the jaw. The mother states that the child sucked well at birth and then the infant appeared to be unable to open its mouth. Stiffness or rigidity of the limbs develops and later the classical spasms begin. In the typical tetanic spasms (which may be brought on by touching the cot, or any part of the patient) the entire body becomes rigid, the arms and legs are extended and the hands are tightly clenched. The face assumes a characteristic attitude (*risus sardonius*) in which the eyes are closed and the corners of the mouth are pulled downwards. In these attacks there may be arrest of respiration with increasing cyanosis. These tetanic spasms may last a few minutes, but even in the intervals between the spasms the body remains rigid and the abdominal wall taut.

There is as a rule no difficulty in diagnosis. Conditions which have to be borne in mind are:

- (a) Intracranial injury.
- (b) Meningitis.
- (c) Tetany.
- (d) Strychnine poisoning.
- (e) Rabies.

The mortality rate is very high; some authorities put it as high as 90%. The longer

the delay in onset after birth the better the prognosis. The first indication of improvement is a lengthening in the interval between spasms.

One of the essentials in the treatment is to disturb the patient as little as possible. Owing to the trismus, it is often necessary to institute gavage feeding. After a preliminary skin test for sensitivity at least 40,000 units of anti-tetanic serum should be given. Half the dose is given intravenously and half intramuscularly. Some authorities even give a small intrathecal dose (10,000 units). Penicillin in large doses is also given. Sedation is a very important part of the treatment and it is aimed at controlling the spasms without causing depression of respiration. The drugs commonly used are:

1. Paraldehyde (either orally, rectally or intramuscularly).
2. Phenobarbitone.
3. Chloral hydrate.
4. Avertin.
5. Magnesium sulphate.
6. Largactil.
7. Myanesin.

Recently, especially in adults, the muscle relaxants have been used. Often this form of therapy necessitates a tracheotomy and thus constant supervision by a team of anaesthetists is essential. In fact, the co-operation of anaesthetists in the treatment of tetanus is

becoming more and more important.

Fortunately the incidence of tetanus neonatorum is being reduced by active immunization.

OPSOMMING

'n Kort verslag oor tetanus neonatorum word verstrek.

Van die 21 gevalle wat gedurende die afgelope

5 jaar in die Coronation-hospitaal behandel is, het net 4 die lewe behou.

Almal was bevallingsgevalle van buite die Johannesburgse munisipale grense. In geen enkele geval was 'n gekwalifiseerde vroedvrou aanwesig nie.

Die beginsels van behandeling word in oënskoue geneem.

Die voorkoms van hierdie kwaal word gelukkig verminder deur aktiewe immunisasie.

DISCOGRAPHY

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The surgical treatment of lumbar disc lesions is directly or indirectly related to degenerative changes in the intervertebral discs.

Clinical methods of diagnosis depend on the patient's history, examination of the lumbar spine and neurological changes in the limbs. They may be supplemented by radiographic evidence of changes in the articulations between the adjacent vertebrae, contrast myelography and lumbar puncture. All these investigations, however, provide indirect evidence about the exact organic state of the disc, and it is only by discography that the changes in the disc itself can be determined radiologically.

This paper presents an analysis of experience gained from a series of 73 discograms on patients with symptoms of degenerative lumbar disc lesions.

Research to demonstrate the nucleus pulposus by radiography was undertaken by Erlacher² in 1949. He showed that when lumbar intervertebral discs were injected with a watery solution of either eosin or methylene blue, the stain showed up only in the nucleus pulposus mass. In the presence of degeneration, when fissures and ruptures directly connected the annulus fibrosus with the nuclear cavity, the area of the annulus took the stain as well. Larger ruptures were frequently filled by the nuclear mass, which could therefore be demonstrated by the stain. Thus the spreading nucleus and its channel of diffusion were made visible, but the nuclear mass alone took the stain.

Staining was then repeated with a watery solution of 0.4% eosin and 30% potassium iodide; this made the impregnation visible radiographically. In all the cases complete agreement was found between the radiographic shadow and the eosin stain, the contours of the stained area being identical with those of

the nucleus pulposus and its diffusion. In no instances were deposits of stain found in healthy or only slightly degenerated areas of annulus fibrosis.

Erlacher conducted further experiments in which he attempted to reproduce the conditions during life by subjecting the disc to a pressure of up to 300 kg. before and after staining. No difference was apparent in these groups.

Finally Erlacher took nucleograms in the living patient, and described various types of disc shapes.

In 1954 Friberg³ mentioned that the radiologist Knut Lindblom had proposed radiological contrast examination of the disc in order to detect the lateral prolapses, or those out of reach of myelography. In their desire to find out from which disc the symptoms emanate, in cases of chronic low back pain, they developed the radiological technique.

TECHNIQUE

Two methods of radiographic technique have been described for taking a discogram in the living patient.

Erlacher uses an extradural type of puncture in which the needle is inserted lateral to the spinous processes, thus by-passing the vertebral foramen at its lateral angle and reaching the disc paradurally.

With this technique it should be possible under normal conditions to remain outside the coverings of the spinal cord. He also demonstrated that, in material taken from post-mortem specimens, after as little as 4 hours the injected solution has diffused to such an extent that it is no longer visible in radiographs. In life absorption is added to diffusion, and the fluid injected at nucleography will disappear completely after a few hours.

Lindblom (quoted by Friberg³) employs a water-soluble contrast medium, and a mixture of 2 c.c. 35% Abrodil (Diotrast) and 0.5 c.c. of 5% novocaine is used. The puncture is made with a double needle; but only the inner needle (diameter 0.5 mm.) is inserted into the disc. The examination is made under fluoroscopic control, and usually includes the fifth, fourth and sometimes the third lumbar disc. Lindblom states that the best route is transdural, close to the midline.

In this series the paradural approach was used in some of the earliest cases. With this method it was found that if the needle is inserted in the plane of the intervertebral disc, one very often strikes the lamina of the vertebra below, making introduction of the needle impossible. With this approach there is also a great possibility that the nerve roots may be pierced, an event which is both dangerous and very uncomfortable for the patient.

A midline transdural approach was subsequently used in all the cases of this series. The lumbosacral, the fourth lumbar disc and, where special indications were present, the third lumbar disc were injected with the contrast medium.

The patient's back is prepared as for a surgical operation, and a meticulous aseptic technique is used throughout. The examination is easier to perform, and is more comfortable for the patient, if half a grain of morphine is administered before the procedure.

The left lateral recumbent position is used with the spine fully flexed, as for a lumbar puncture. The fourth and fifth lumbar spines are palpated, and local anaesthetic is injected in the midline just below these spines. While the needle remains in position, it is useful to take a lateral recumbent radiograph for general orientation. A fine lumbar puncture needle at least 10 cm. long, which can be fitted to a Luer-Lok syringe with 3 finger rings, is used, as very often considerable pressure is necessary for the injection. The needle is inserted transdurally, in an upward direction, to the posterior aspect of the vertebral bodies, and its position is radiographically determined by means of a lateral recumbent X-ray. By altering the position of the needle, if necessary, the disc itself can next be penetrated, and the needle is then inserted up to the posterior third of the disc, as demonstrated by a further lateral radiograph. With a little experience one soon learns the feel of the rubbery annulus fibrosus, and it is often possible to insert the needle correctly at the first

attempt.

It is necessary to insert all the needles before the injection of the contrast medium, and to inject the solution with as little delay as possible. Once the needles are in position, the discs are injected with a 50% Pyelocil solution. The amount may vary from 0.5 c.c. to about 3 c.c. according to whether the disc is degenerated or not. Where a complete rupture of the annulus fibrosus has occurred, the Pyelocil is dispersed extradurally, and in these cases a virtually unlimited amount can be injected.

Antero-posterior, lateral and right and left oblique views should be taken as quickly as possible, for the contrast medium diffuses quite rapidly.

It has been found useful, when taking the antero-posterior view, to direct the tube so that it lies in the same plane as the lumbosacral disc.

TECHNICAL DIFFICULTIES

In several of the cases it was found that the contrast medium was so rapidly absorbed, that instead of

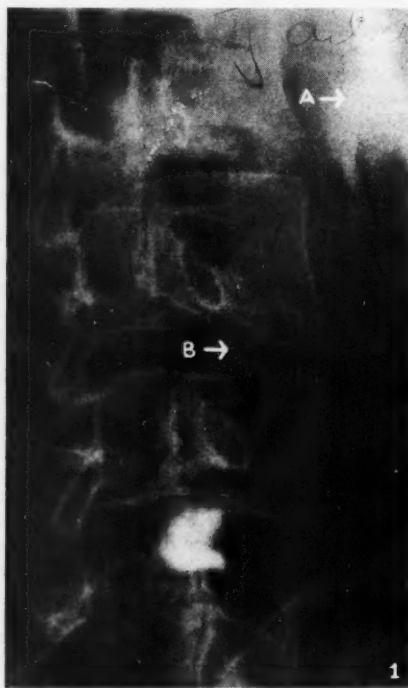


Fig. 1. The outline of the renal pelvis is indicated by the arrow at A. There is no outline of the nucleus (B).

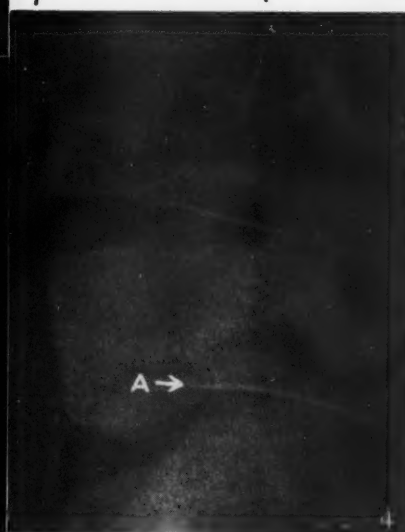
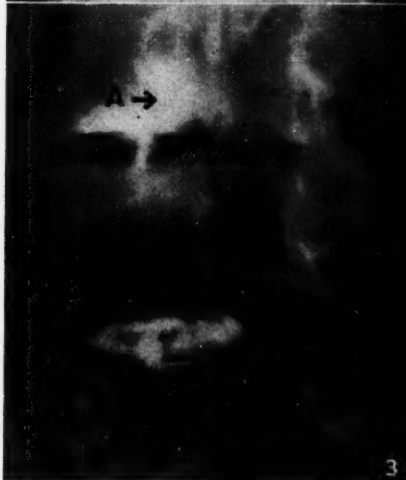
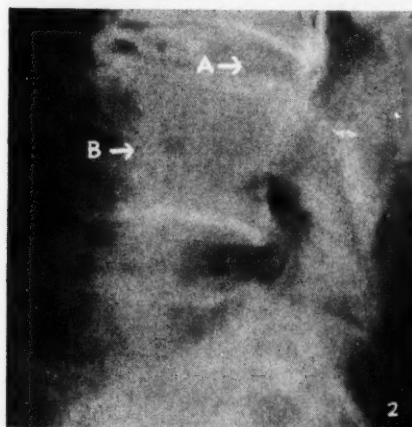
the nuclear contours being outlined, a pyelogram could be demonstrated (Fig. 1). This happened even if the radiographs were taken simultaneously with the completion of the injection.

The only possible route of absorption is via the richly vascularized vertebral body, and a closer inspection revealed that in these cases the point of the needle was not lying in or near the centre of the nucleus, but had actually penetrated the cartilage end-plate of the vertebral body.

In a case where this occurred, a radiograph was taken simultaneously with the injection of the contrast medium. The nucleus was not outlined, but a faint line of contrast medium branching across the vertebral body indicated the route of absorption (Fig. 2).

A Schmorl's node is usually clearly outlined, indicating that absorption takes place much more slowly from the avascular nuclear material, even if its lies within the vertebral body (Fig. 3).

With this technique it is impossible to insert the needle in the same plane as the intervertebral disc, because the spinous process of the vertebra above is in the way. The plane in which the needle is



Figs. 2, 2a.

A. Multiple branched nucleus.

B. Outline of contrast medium branching across the vertebral body.

Fig. 3. Outline of a Schmorl's node indicated by the arrow at A.

Fig. 4. The tip of the needle perforating the cartilage end plate is indicated by the arrow at A.

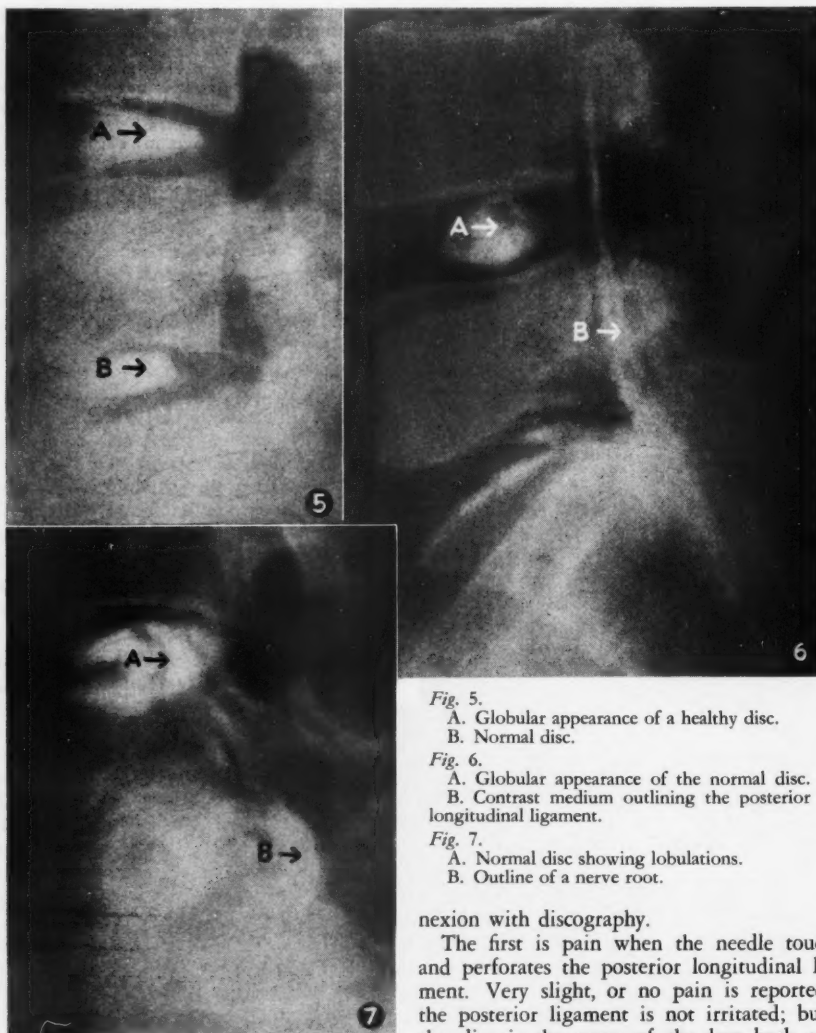


Fig. 5.

- A. Globular appearance of a healthy disc.
B. Normal disc.

Fig. 6.

- A. Globular appearance of the normal disc.
B. Contrast medium outlining the posterior longitudinal ligament.

Fig. 7.

- A. Normal disc showing lobulations.
B. Outline of a nerve root.

nexion with discography.

The first is pain when the needle touches and perforates the posterior longitudinal ligament. Very slight, or no pain is reported if the posterior ligament is not irritated; but if the disc is the cause of the low back pain, the ligament is very sensitive.

The second symptom is pain when the cavity of the disc is distended by the contrast medium. Injection in a normal disc provokes a slight pain at the level of the injection, but distension of a degenerated disc often accentuates the patient's clinical symptoms.

When this investigation was started the contrast medium was mixed with novocaine, as suggested by Lindblom. Later on this was not done, and it made absolutely no difference to the symptoms experienced by the patient. It was also found, in contrast to Friberg's find-

inserted therefore meets the plane of the intervertebral disc at an angle. In the lumbo-sacral disc the angle is still greater, and if the intervertebral space is narrowed as well, the point of the needle may penetrate the cartilage end-plate covering the inferior aspect of the fifth lumbar vertebra (Fig. 4).

In this event the needle should be inserted again so that it lies in or near the centre of the nucleus. This will ensure that the contrast medium is not absorbed, and that the nuclear material is clearly outlined.

SYMPTOMS IN CONNECTION WITH DISCOGRAPHY

Friberg mentions two symptoms noted in con-

ings, that the contrast medium could often be injected with ease into a degenerated disc, and the patients seldom experienced severe pain.

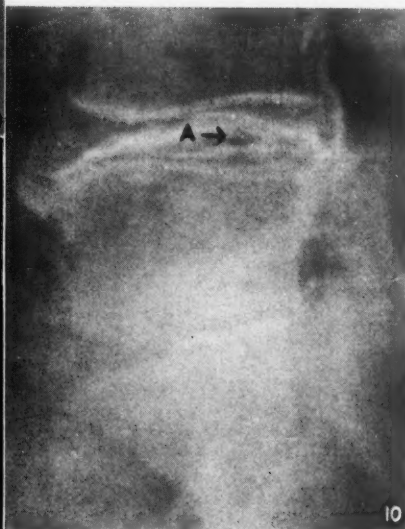
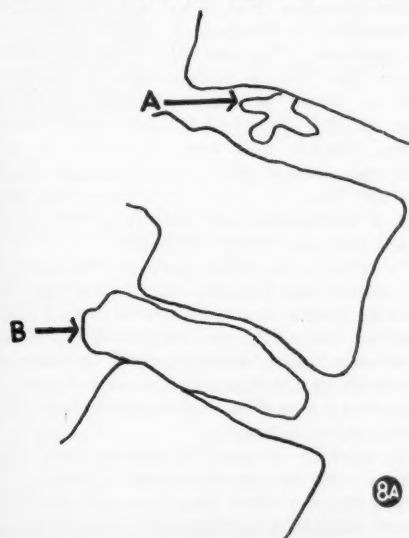
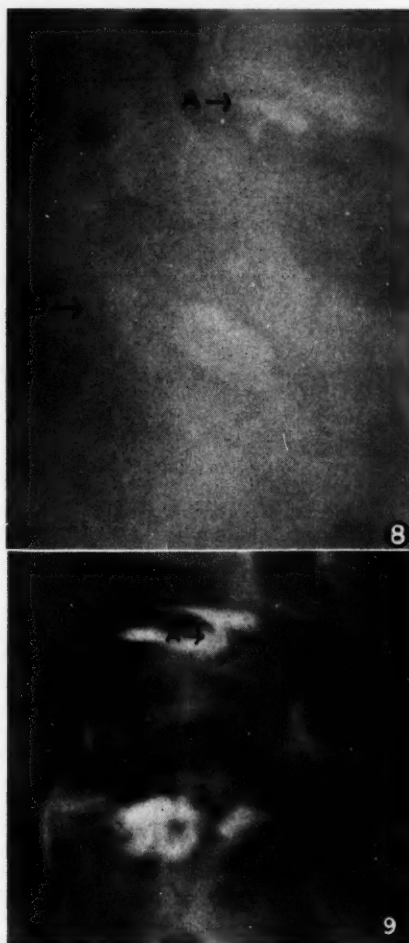
It seems, therefore, that, it is impossible to draw any conclusions about the state of the disc from the symptoms experienced by the patient during the injection of the contrast medium.

INTERPRETATION OF RADIOGRAPHS

Some experience is necessary to interpret the

radiographs correctly. In all cases it is essential to study the antero-posterior, lateral and oblique views closely before any conclusions are drawn.

A healthy disc without degeneration or herniation has a globular appearance in young



Figs. 8, 8a.

A. Branched nucleus.

B. Retropulsion.

Fig. 9. The branched nucleus is indicated by the arrow at A.

Fig. 10. The multiple branched nucleus is indicated by the arrow at A.

subjects [Figs. 5 and 6 (L4-L5 disc)].

In adults a healthy disc may show a few lobulations [Fig. 7 (L4-L5 disc)].

A degenerated disc may show various appearances. The simple branched nucleus shows a central shadow with a few long and narrow branches (Figs. 8 and 9, L4-L5 discs).

According to Erlacher, this type predisposes to herniation. The case illustrated in Fig. 8 shows this type of nucleus between L4-L5 and an actual herniation between L5-S1. The multiple branched nucleus has a small central shadow, and several branches in all directions, instead of the central shadow (Fig. 10 and Fig. 2). This form represents the typical degenerated disc and is mostly associated with narrowing of the disc.

In actual retropulsion parts of the nucleus are outside the disc and the contrast shadow projects clearly beyond the margins of the vertebral bodies. In the antero-posterior view a medially situated herniation will be covered by the central nuclear shadow, and this type of herniation is shown most distinctly in the lateral view (Fig. 8).

A laterally situated herniation will be noticed on the corresponding side in the antero-posterior view, but is brought out best in the oblique view (Fig. 11).

With free prolapse, connexion with the central shadow can, in many instances, no longer be demonstrated, and the prolapse shadow, with indistinct contours, is situated beyond the disc (Fig. 12, L5-S1 disc).

It often happens that the contrast medium

escapes extradurally in the presence of a ruptured annulus. In these cases the contrast medium may outline the posterior longitudinal ligament (Fig. 6) or the nerve roots, as is very clearly demonstrated in Fig. 13.

When the nerve roots are outlined, this may give rise to difficulties in the interpretation of the radiographs. In the oblique view (Fig. 7) the contrast shadow was interpreted as presenting a lateral prolapse at the L5-S1 level.

When no prolapse was found at operation, a closer study of the various views in combination showed that the contrast medium had escaped extradurally along the S1 nerve root. This was clearly demonstrated in the antero-posterior view, and gave the impression in the oblique view of a laterally situated herniation.

The contrast medium may also escape extradurally along the needle tract (Fig. 14), and the contrast medium shadow then outlines the posterior longitudinal ligament.

In these cases the shadow outlining the bulge of the posterior longitudinal ligament should not be confused with a free-lying prolapse, and it should be kept in mind that the actual contour of the annulus fibrosus lies in front of this shadow. The different views should therefore be carefully studied in combination before the diagnosis of a retropulsion is made.

CLINICAL VALUE OF DISCOGRAPHY

The diagnosis of a retropulsion of a lumbar intervertebral disc can be made fairly definitely

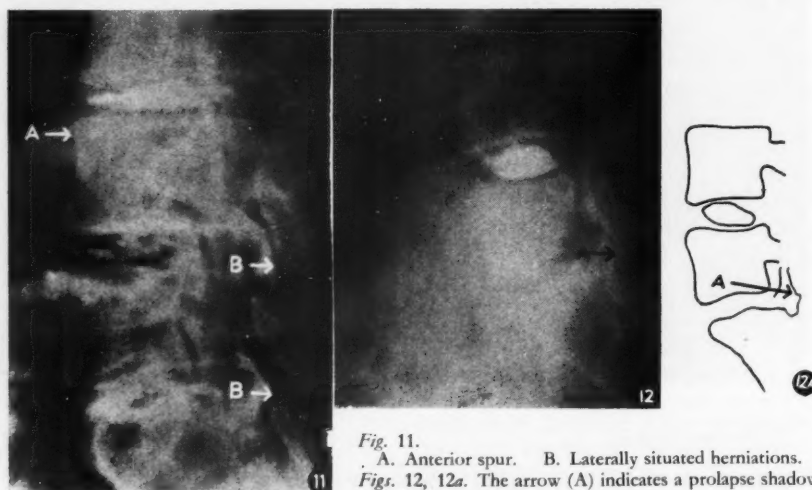


Fig. 11.

A. Anterior spur. B. Laterally situated herniations.

Figs. 12, 12a. The arrow (A) indicates a prolapse shadow with indistinct contours.

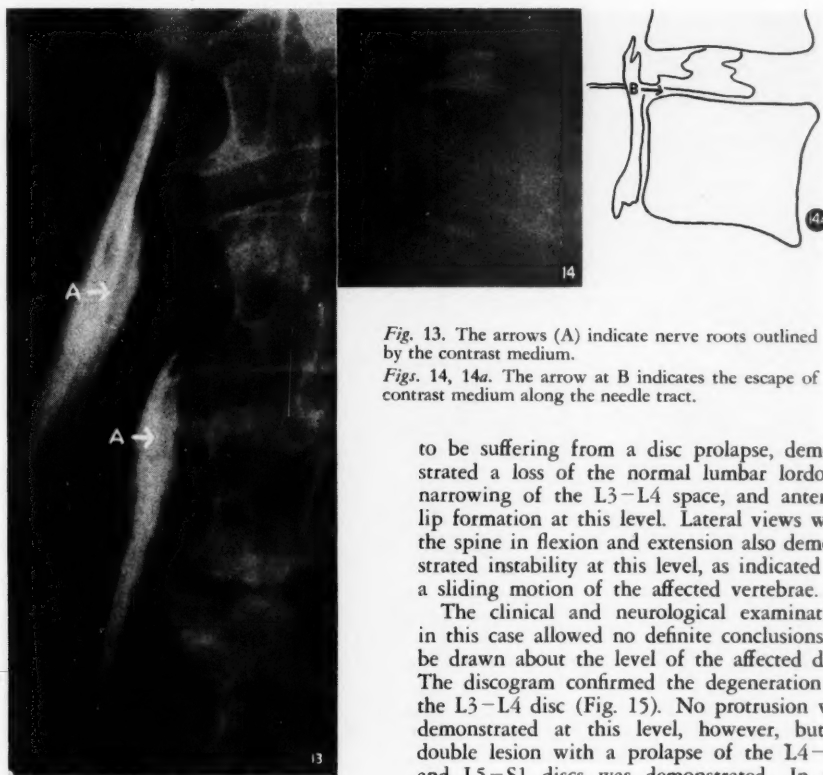


Fig. 13. The arrows (A) indicate nerve roots outlined by the contrast medium.

Figs. 14, 14a. The arrow at B indicates the escape of contrast medium along the needle tract.

on clinical grounds. A direct indication of the organic state of the disc, as demonstrated by discography, provides additional information, and in this series has proved to be of value in the following instances.

1. A discogram fixes the exact level of the disc involved, whereas the clinical determination of the affected level may be, and often is, fallible.

The site of a disc lesion is determined mainly by the clinical pattern of root involvement on the assumption that the patient has a normal lumbar plexus and 5 mobile vertebrae in the lumbar region. A pre- or post-fixed lumbar plexus as well as variations in the number of mobile lumbar vertebrae are fairly common, and the level at which the extra-thecal nerve roots emerge may also differ on the corresponding sides in the same patient.

The fallibility of the clinical determination of the affected level is well illustrated in the following cases.

The plain lateral view of a patient diagnosed

to be suffering from a disc prolapse, demonstrated a loss of the normal lumbar lordosis, narrowing of the L3-L4 space, and anterior lip formation at this level. Lateral views with the spine in flexion and extension also demonstrated instability at this level, as indicated by a sliding motion of the affected vertebrae.

The clinical and neurological examination in this case allowed no definite conclusions to be drawn about the level of the affected disc. The discogram confirmed the degeneration of the L3-L4 disc (Fig. 15). No protrusion was demonstrated at this level, however, but a double lesion with a prolapse of the L4-L5 and L5-S1 discs was demonstrated. In the oblique view (Fig. 11) the double protrusions are clearly shown, as well as the anterior spur formation at the upper anterior border of the fourth lumbar vertebra. These findings were confirmed at operation.

In the other case a patient complained of persistent low back-ache which was referred to the anterior superior iliac spine. Clinical examination and plain X-rays did not reveal a disc lesion. A discogram was done after various prolonged methods of conservative treatment had been tried. A large posterior protrusion of the L5-S1 disc was demonstrated (Fig. 8), and this was confirmed at operation.

2. The size and position of a retropulsion of the nucleus pulposus can be determined by means of discography. In Figs. 11 and 16 lateral protrusions are shown in the oblique views. With this information, an exposure which is developed far laterally facilitates the removal of the disc.

3. According to Armstrong¹ both the L4-L5 and L5-S1 discs are affected simultaneously in between 10-20% of all patients.

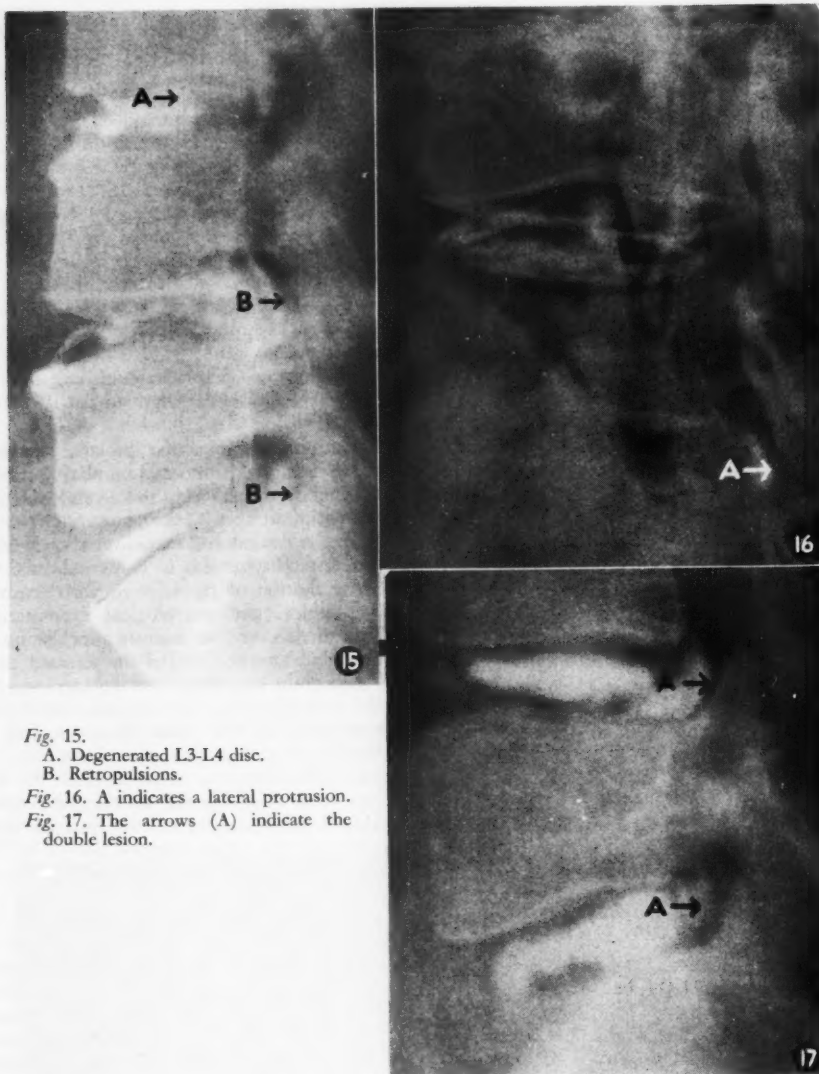


Fig. 15.

A. Degenerated L3-L4 disc.

B. Retropulsions.

Fig. 16. A indicates a lateral protrusion.

Fig. 17. The arrows (A) indicate the double lesion.

The presence of such a double lesion cannot always be recognized clinically and if, in these patients, one disc only is exposed and dealt with, residual symptoms produced by the second lesion are inevitable.

Double lesions are demonstrated in Figs. 15 and 17.

4. It is customary during a laminectomy to explore more than one space, but if on discography the disc is normal, pathology can be

ruled out, and only the abnormal disc need be explored. This reduces the operating time and avoids unnecessary trauma to the patient's back.

5. Low back pain may to a great extent be attributable to degenerative changes in and around the lumbar discs, and to lumbar vertebral instability. This instability or sliding motion of the vertebral bodies is an early sign of lumbar disc degeneration without retropul-

sion, which may be present long before there is any appreciable diminution in disc volume as shown by the narrowing of the joint space. As a result of the instability with excessive mobility, further damage occurs to the annulus fibrosus, the inter- and supra-spinous ligaments, the ligamentum flavum and the paravertebral joints. In cases of lumbar instability, discography may disclose the space in which the low back pain originates, even when the clinical findings are negative, and before changes in the plain radiographs are present.

6. Harris and Macnab⁴ have shown that

subluxation and deforming arthritis of the paravertebral joints which follows on disc degeneration may actually compress the nerve in its exit from the intervertebral foramen. Such a case is shown in Fig 10. There is marked narrowing of the joint spaces, and disc degeneration but no retropulsion is indicated on the discogram, suggesting some other cause for the root involvement in this patient. At exploration the S1 nerve root was found to be compressed by the superior articular process of S1.

7. There is a formidable list of other con-

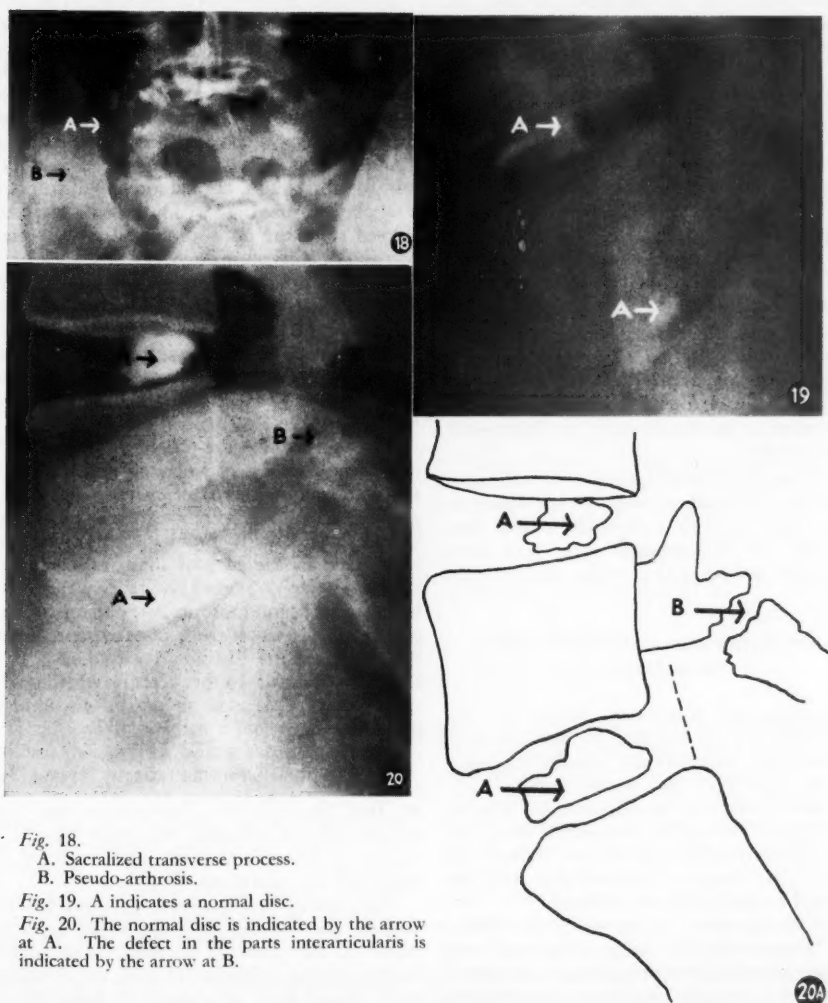


Fig. 18.

- A. Sacralized transverse process.
- B. Pseudo-arthritis.

Fig. 19. A indicates a normal disc.

Fig. 20. The normal disc is indicated by the arrow at A. The defect in the parts interarticularis is indicated by the arrow at B.

ditions simulating posterior herniation of the nucleus pulposus, and discography may help in confirming or disproving the diagnosis of disc pathology.

(a) It is by no means uncommon to find a lumbar disc lesion in association with, but at a level other than a spondylolisthesis. If the disc lesion is overlooked and the patient's symptoms attributed to the spondylolisthesis only, this error may have most unfortunate results if the patient is then treated by spinal fusion.

Clinically association of these lesions may be suspected, but a discogram will provide direct evidence that this is the case. A case of spondylolisthesis without associated disc lesions is shown in Fig. 20.

(b) A sacralized transverse process with an arthritic pseudo-arthritis is an uncommon condition, but it may be associated with root irritation. The difficulty is to decide whether this condition or an associated disc lesion is responsible for the patient's symptoms. A sacralized transverse process with a pseudo-arthritis is shown in Fig. 18. The discogram (Fig. 19) of this patient clearly indicates that his root symptoms cannot be attributed to an associated disc lesion.

(c) The presence of osteoarthritis, even in a marked degree, by no means excludes the possibility of an associated disc lesion. In several of the cases in this series a disc lesion in the presence of osteoarthritis was confirmed by discography.

(d) Spondylitis ankylopoietica in the very early stages is another condition in which it is not always possible to exclude a mild disc lesion of the degenerative type, and here discography should prove useful in differentiation.

COMPLICATIONS IN CONNEXION WITH DISCOGRAPHY

1. *Complications from the Effect of the Injected Solution.* It has been shown in several thousand cases of deliberate intrathecal injection (myelography) that watery iodine solutions will cause no arachnoidal or similar disturbances. The iodine is absorbed from the theca and excreted rapidly by the kidneys. In this series no reactions occurred that could be attributed to the contrast medium.

2. *Complications as a Result of the Puncture.* Theoretically it is possible that the puncture may facilitate herniation at the point of entry of the needle. Erlacher's experiments,

in which the discs were subjected to a pressure of 300 kg., have never shown this to occur.

Friberg also tried to produce disc prolapse experimentally by exposing lumbar spine specimens to severe strains. These experiments revealed that unless a portion of the disc had already been detached, even relatively large defects in the fibrous ring did not lead to herniation of the nucleus.

In this series over 156 discs were injected. Many of these were subsequently removed, but so far no evidence has been found that herniation occurred in any of the remaining discs as a result of the puncture.

The discs exposed at operation a few days after discography were carefully examined for signs of damage as a result of the puncture, but in no case could the puncture hole be recognized.

One patient was treated operatively a year after discography had revealed a herniation of the lumbo-sacral disc. The L4-L5 disc, which was interpreted as normal on the discogram, was also exposed and although a year had elapsed since the puncture, the disc was interpreted as being normal.

Several discs interpreted as normal on the discogram were injected with normal saline at operation. This was done in patients who had discs removed for herniation at other levels. Although considerable force was used, the saline solution did not even leak past the needle.

It is possible that the procedure might facilitate herniation if a degenerated disc with only a few remaining fibres of annulus fibrosus is punctured. This is a point to keep in mind, should medico-legal problems arise, as they have done in the case of lumbar punctures.

3. *Infection.* Symptoms that were attributed to infection arose in two patients of this series. The discs in these cases were removed the day after the discogram was done. It is therefore difficult to be certain whether the infection arose as a result of the discography or of the operation.

DISCUSSION

In this investigation discography was performed on 73 patients and more than 156 lumbar intervertebral discs were injected by means of the technique described.

The contrast medium used was entirely satisfactory, and no complications could be attributed to the contrast medium itself. If a careful aseptic technique is used, no complications should arise as a result of infection.

Theoretically it is possible that the puncture may facilitate herniation, but this complication has not occurred in any of the patients in this series, although the longest follow-up has been just over 2 years.

Laminectomy was only performed if the accepted indications for operative treatment were present, and when the discogram demonstrated a retropulsion of the nucleus. In all the cases where the discogram was correctly interpreted, the presence of a posterior herniation could be demonstrated at the levels and positions indicated by the discogram. The discs that were interpreted as being normal on the discogram were also explored, and in every instance the absence of a herniation was confirmed at operation. So much reliance is now placed on this investigation that only the abnormal discs, as demonstrated on the discogram, are explored, thus reducing the operating time and avoiding unnecessary trauma.

Discography has proved to be of value in those cases which present with atypical signs and symptoms, and to confirm or disprove the diagnosis of disc pathology in the presence of other conditions simulating posterior herniation of the nucleus pulposus.

Discography may give positive results when the plain radiograph and the myelogram are negative. By discography it is also possible to show the shape of a posterior herniation, as well as its position. In the myelogram small and laterally situated herniations are frequently not shown.

At this stage it is still impossible to say whether discography should be employed routinely for cases in which operative removal

of a disc herniation is contemplated. In this series the examination has proved to be of undoubted value in the diagnosis and treatment of lumbar disc lesions.

SUMMARY

1. The development of discography, and the various techniques employed to demonstrate the nucleus pulposus by contrast radiography, are discussed.

2. Various types of radiographic appearances of degenerated lumbar discs are illustrated and described.

3. The complications and the clinical value of the procedure are discussed.

I am indebted to Mr. J. G. du Toit for his permission to submit this report for publication, for his encouragement and for the interest which he has taken.

OPSOMMING

1. Die ontwikkeling van diskografie, en die verskillende metodes wat gebruik word om die skyfkerne radiologies te demonstreer, word bespreek.

2. Die radiologiese voorkoms van verskillende tipes ontaarde lenden tussenwerwelskywe word illustreer en beskryf.

3. Die komplikasies en kliniese waarde van die ondersoek word bespreek.

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DYSPEPSIA: CLINICIANS AND RADIOLOGISTS*

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I was in general practice myself long enough to realize that dyspepsia is a subject on which every general practitioner is an authority. As a clinician, I would have found it a very difficult subject to discuss with a gathering such as this; for the radiologist, it is the happiest choice of topics. In other branches of radiology it suits one's purpose to get to know as much about the X-ray appearance of disease as possible. One may then use the radiologist's

report, when needed, as one uses a travel guide book, critically, adding one's own observations and drawing one's own conclusions.

In gastro-enterology the radiologist has the distinct advantage of being able to examine the live, moving organs under direct vision, by inspection and palpation. He satisfies himself about such features as flexibility, pliability, mobility and the relationship of palpable masses to visible organs. He gains a fleeting glimpse now and again of appearances not recorded on the radiographs. The report on a

* Based on a lecture at the Post-Graduate Refresher Course, Durban.

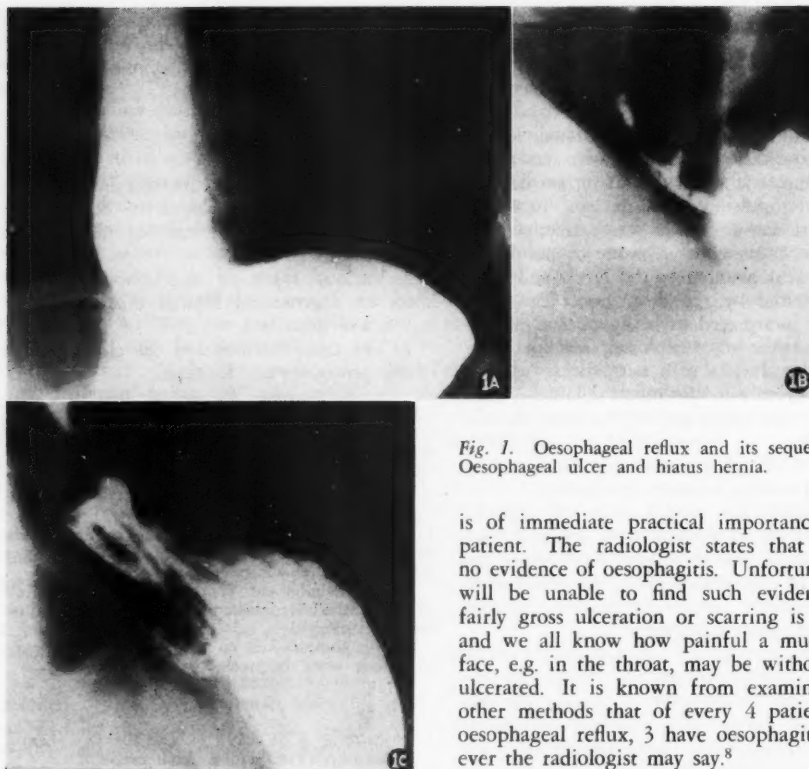


Fig. 1. Oesophageal reflux and its sequelae. Oesophageal ulcer and hiatus hernia.

is of immediate practical importance to the patient. The radiologist states that there is no evidence of oesophagitis. Unfortunately, he will be unable to find such evidence until fairly gross ulceration or scarring is present,⁵ and we all know how painful a mucous surface, e.g. in the throat, may be without being ulcerated. It is known from examination by other methods that of every 4 patients with oesophageal reflux, 3 have oesophagitis, whatever the radiologist may say.⁸

barium meal then becomes a fuller guide to the clinician. Unfortunately, these reports teem (and you may have been in practice long enough to be well aware of it) with half-truths and sometimes with apparent untruths. I submit a few such reports, accounts of barium meal examinations on patients with dyspepsia, for discussion and criticism.

1. 'There is free regurgitation of barium into the oesophagus, but no radiological evidence of oesophagitis at present.' (Fig. 1). The report sounds deceptively harmless. The fact is that the finding of free oesophageal reflux is more important than the demonstration of a small hiatus hernia.^{6,7} Oesophageal reflux should lead to examination of the fasting gastric contents⁸ and repetition of the barium meal examination months or years later, depending on progress. The follow-up examination is necessary, of course, because acid regurgitation is the precursor of oesophagitis and peptic ulceration of the oesophagus, and likely to lead in time to hiatus hernia.

Apart from later complications, the report



Fig. 2. A chronic, active duodenal ulcer.

2. 'A chronic, active ulcer crater is present in the duodenal cap.' (Fig. 2). I used to be a little sceptical about reports like this one. Can the radiologist really presume to demonstrate chronicity of an ulcer on a single examination? If contracture of scar tissue is accepted as indicating chronicity, it can be clearly displayed. Gross contracture of the duodenal cap apart, chronicity is commonly represented by a puckering of the mucosa into radiating folds around the crater.

Activity is usually indicated by surrounding oedema, which produces a halo round the ulcer seen end-on.

These features are, of course, significant in



Fig. 3. A large gastric ulcer on the lesser curve, with raised margins.

Fig. 4. Duodenal diverticula. These are often not responsible for the patient's discomfort.

the planning of further treatment, and may be of great importance in deciding between medical and surgical treatment.

3. The radiologist reports that the large chronic ulcer on the lesser curve of the stomach, with its thick, raised edge is probably malignant (Fig. 3).

Histological examination after gastrectomy shows it to have been a chronic, simple peptic ulcer. The mistake is not an uncommon one. The radiological criteria for distinguishing between benign and malignant ulcers are proved to be unreliable with monotonous regularity.^{4, 10-12}

It may be reassuring to know that the radiologist is constantly on the alert to detect any sign that may suggest malignancy, and is more liable to suspect the benign than to trust the malignant lesions.^{1, 10}

4. 'Severe pylorospasm is present. No ulcer could be demonstrated.' This type of report probably annoys the practitioner who receives it. Pylorospasm is also the bane of the radiologist's existence. We struggle with it almost daily. It has numerous causes, apart from gastric and duodenal ulceration, including disease in and outside the gastro-intestinal tract, as well as purely psychological disturbances.

The report states that an ulcer was not demonstrated. Duodenal ulcers and sometimes even gastric ulcers may defeat radiological detection, for such reasons as a crater obscured by oedema or filled with blood clot, or simply small size.^{4, 9}

How then should one handle a case like this? 'No ulcer could be demonstrated'. The first step may not unreasonably be to telephone the radiologist. Although the report is non-committal, he may be able to say whether on this particular occasion the mucosal surface of the duodenal cap could be demonstrated clearly enough for an ulcer to be excluded with a fair degree of certainty. If not, the usual procedure is to treat the patient as for an ulcer, and to repeat the barium meal examination after an interval.

5. Duodenal Diverticula (Fig. 4).

We are sometimes so eager to find an organic cause for a patient's symptoms, that we are inclined to clutch at any straw for an explanation. Certainly, duodenal diverticula can and do cause symptoms, because they may become inflamed and ulcerated, or they obstruct the pancreatic duct, the common bile duct, and even the duodenum itself. However,

the vast majority are silent, and the finding of a moderate sized diverticulum which drains or empties itself freely, should not terminate the search for the cause of dyspepsia.

So much for these few examples. I do not pretend that the reports you receive are similarly worded. I do not even pretend that the few facts we have mentioned are worth remembering. I would be completely satisfied if I have demonstrated to your satisfaction that the radiologist's report suffers from the falsity of over-simplification, and that the time spent on a discussion with him is often not wasted. The radiologist welcomes nothing more than closer contact with the clinician and the opportunity of discussing the case and his report with the clinician.

Finally, to put the cart before the horse, a few words on when we feel radiological examination to be necessary in carcinoma, typical peptic ulcers and functional dyspepsias.

1. About carcinoma nothing more need be said. I have yet to meet the practitioner who fails to investigate the middle-aged patient fully on the first dyspeptic symptom.

2. The position is perhaps a little different regarding typical peptic ulcers. When I was in general practice, I sometimes treated patients with a classical peptic ulcer history without roentgen investigation, usually for financial reasons. The following two of many examples illustrate why such an attitude may be unwise.

(a) Hiatus hernia often does not give rise to typical symptoms. The commonest symptom, in fact, is epigastric pain.³ We need not be surprised if our peptic ulcers occasionally turn out to be cases of hiatus hernia.²

(b) Every radiologist in his search for peptic ulcers stumbles occasionally upon gall stones. Because only 10% of gall stones are radio-opaque, for every case uncovered in this way, 9 may be missed. The discovery of cholecystitis as a cause of indigestion cannot be left to chance.

3. I had the usual number of functional dyspepsias in practice, and I often failed to give them the benefit of a radiological exami-

nation. Apart from the reassuring value of demonstrating to a nervous patient the absence of a cancer, I have been surprised, often enough, even in my short experience in radiology, by the finding of organic disease in frankly neurotic patients. I feel that if I had to handle these functional dyspepsias again to-day I would make quite sure that their first X-ray was not the one taken to demonstrate free air in the peritoneal cavity.

My thanks are due to Dr. Margaret Findlay and to Dr. N. Sacks, heads of the Radiology Departments of the King Edward VIII and Addington Hospitals respectively, for instruction and for the use of films from their museums.

Mr. Stuart of the Durban Medical School kindly prepared the photographic reproductions.

OPSOMMING

Die probleem van dispepsie soos gesien uit die standpunt van die klinis en die radioloog word deur die skrywer in oënskou geneem.

Hy vestig die aandag op die beperkte waarde van 'n radiologiese verslag *per se*, en lig sy tesis toe met voorbeelde wat die klem laat val op die belangrikheid daarvan om die radiologiese waarnemings met die kliniese bevindings te korreleer voordat die probleem wat deur die pasiënt gestel word, na waarde bepaal kan word.

Die skrywer oorweeg ten slotte wanneer radiologiese ondersoek noodsaaklik is in gevalle van karsinome, tipiese peptiese swere en funksionele dispepsie.

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ENDOGENOUS ENDOCRINE ALLERGY

CONCEPT AND THERAPY

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In the investigation of cases of possible allergy it is seldom that the physician asks his patient

whether the complaint has been in any way related to the major hormonal milestones, to

puberty, menstruation, pregnancy or the climacteric. This question, if asked, would uncover the problem of endogenous endocrine allergy, sometimes called autogenous hormonal allergy.¹⁻⁶ By the use of the word 'endogenous' a distinction is drawn from the exogenous form of endocrine allergy, resulting directly from sensitivity to hormones given for treatment.

Endogenous allergy results not from substances introduced from outside but, as the name implies, from a sensitivity to circulating hormones as they are produced in the physiological functioning of the body, because of some peculiarity of quantity or quality. The sensitivity therefore has a definite cyclical time or physiological relation to the functioning of the endocrine glands. It is demonstrated by skin reaction tests with the suspect hormones, and treated by various techniques of desensitization.

Endogenous endocrine allergy has been described as a 'subject 'intriguing and poorly understood';⁶ yet 'supported by evidence extensive enough to have obtained general acceptance, its place in therapy is still to be evaluated'.⁷

It is in that spirit that this paper must be presented. It is the clinical record of the experiences of our group of doctors in the investigation and treatment of selected cases over 7 years. This we have placed against the background of the literature as we have read it. By presenting our cases as we have seen them, we hope to make a more genuine contribution than by posing as theoretical allergists or endocrinologists.

We are satisfied that the system of investigation and treatment which we have followed has offered to a limited number of cases (because endocrine allergic conditions are not frequent) diagnosis, treatment and, at times, cure, which they would otherwise have been denied. We feel that our treatment rate of cure or improvement of approximately 60% is worth while. But we, as others in this field,^{4,6} have encountered case problems with no easy solution.

History. The conception of a body sensitive to products of its own physiology has been one which many clinicians have found difficult to accept. However, in recent years the existence of such a sensitivity has become firmly established.

Calveti⁸ states:

'The concept of autoimmune disease comprises conditions which are due to the pathogenic effects of antibodies produced by an individual against components of his own tissues. The existence

of such conditions in man has been established beyond doubt.'

For example, we accept sympathetic ophthalmia, after damage to the uveal tract, as due to the allergic response of the patient to his own uveal pigment; paroxysmal haemoglobinuria as due to autohaemolysins produced on exposure to cold⁶; and experimental encephalomyelitis in the monkey as a true antigen-antibody reaction, resulting from the injection of homologous brain tissue.

When we pass to consideration of a body sensitive to the products of its own endocrine system, we must begin with the original work of Geber in 1931.⁹ He took a patient suffering from premenstrual urticaria, obtained the serum at that time, injected it intravenously during the intermenstruum, and produced urticaria. Premenstrual serum from normal controls did not invoke this response. He reasoned that there were substances in the patient's blood at the premenstruum to which she was sensitive, and he successfully desensitized his patient with her own serum. Several other investigators have since confirmed his findings.^{10, 14-16}

The two excellent papers of Zondek and Bromberg^{1, 2} are corner-stones in the present-day conception of endogenous endocrine allergy.

In these papers they reported that they had been able to demonstrate:

1. Skin-sensitivity reactions to suspect hormones;
2. The development of local antibodies at the injection site;
3. The production of specific antibodies in the serum and their passive transfer—a reagin reaction similar to those of allergic reactions in general. Further, they were able to record notable therapeutic results following desensitization with the indicated hormone.

Our own work (as that of many others¹¹⁻¹³) has been stimulated by them and has followed the pattern as they laid it down. That pattern is:

1. The patient to be studied must give a history which suggests a direct relationship between the complaint and the hormonal cycle.
2. Exogenous allergens must be excluded by routine tests.
3. Skin sensitivity tests must be performed with pure crystalline hormones.
4. The skin reactions must be read as 'immediate' (within 48 hours), 'retarded' or 'recurrent' reactions.
5. Therapy by desensitization is begun on positive skin reactions only.
6. The manner of treatment is usually by percutaneous injection of minimal quantities of the suspect hormone, but it may be achieved by other methods.

The full details relative to these requisites can be obtained from the original papers.

Although a great deal has been written by others since, and many problems raised,^{4,5} the original theory and therapy of Zondek has not been displaced. Two important differences in concept have been raised by Solari and Heckel.

Solari and his co-workers in the Argentine,⁴ who prefer the term 'autogenous hormonal allergy' to 'endocrine allergy', have suggested that this allergy may be initiated by substances related to the hormones chemically which are ingested or otherwise acquired. By these steroid substances the patient will be allergized. When the cyclical increase of the endogenous hormones crosses a certain tolerance threshold, the allergic reaction will be produced. This explanation obviously requires much review, but typifies the attempts to uncover a shadow substance which will be the true allergen, with the endogenous hormone a 'loosing' or 'trigger' factor only.

Heckel⁵ may have come near this substance. He was impressed by the trouble all investigators have encountered in the considerable variation in the sensitivity of the skin.⁶ It is a frequent finding that the skin may respond to several substances at one testing, or different substances at different testings. Heckel believes that pregnandiol, the excretion product of progesterone, is the 'shadow substance' and chief hormonal agent.

We feel, from our own observations and those of our interested colleagues, that future investigation should stress the skin testing of pregnandiol and chorionic gonadotrophin and we are at present investigating patients along these lines. The purpose and discussion of this paper will, however, best be served by a direct comparison of our experiences with those in the original report of Zondek.

PRESENT SERIES INVESTIGATION

Beginning in 1948, we investigated all cases whose history suggested that their allergy might be associated with their hormonal fluctuations. Investigation has been largely limited to the female because of the obvious advantage of a clear cycle to which events could be related.

The conditions which we have investigated and treated have been:

Migraine;	Recurrent conjunctivitis;
Vasomotor rhinitis;	Menorrhagia;
Asthma;	Generalized pruritus;
Urticaria;	Pruritis ani and vulvae;
Acne;	Recurrent stomal ulcers;
Keratitis;	Intermittent hydrarthrosis.

It is interesting to compare these conditions with the series of Zondek.^{1,2} Stomal ulcers

and intermittent hydrarthrosis were not treated by him; but premenstrual tensions, premenstrual fever and chronic eczema were.

The series of Heckel⁵ embraced a further field, including painful breasts, ovarian pain syndrome and endometriosis.

SKIN SENSITIVITY REACTIONS

Zondek tested 216 women for sensitivity to hormones; 32 of them were in good health with regular periods and none gave a positive reaction to hormones; 68 suffered from disturbances not associated with the genital function and 2 (3.3%) showed positive responses; 116 had complaints related to menstruation or the menopause, and of these 73 (63%) had positive responses.

These tests were performed only, as in our own cases, when routine investigations had excluded exogenous allergens.

Heckel, using pregnandiol, obtained positive reactions in 74% of women with premenstrual distress, in 60% of those with painful breasts, in 56% of patients with menopausal symptoms, and in 56% with the ovarian pain syndrome.

In our series we have no normal controls, for we were dealing only with the therapeutic aspect. We chose those cases who clearly stated that their symptoms arose in relation to their periods, who were completely free of previous symptoms during pregnancy or who definitely dated their trouble from puberty or the menopause.

We have tested 148 women in the groups already listed, as well as 3 women with premenstrual epilepsy and 3 men. The endocrine approach was suggested in the 3 men investigated because, in the first, his mouth ulcers had begun at puberty; in the other two their symptoms (arising later in life) had followed a sudden drop in libido. The 3 women with premenstrual epilepsy all showed negative responses and were therefore not treated by desensitization.

Of our total of 154, 90 gave positive skin responses, 21 by the retarded reaction. The percentage of positive reactors in our series is therefore 58% as compared with 63% in that of Zondek.

Skin Sensitivity Tests: Technique. The tests must be made with preparations of pure crystalline hormone. Until lately these have been difficult to obtain, so that our range of skin tests has been limited to oestrone, progesterone, testosterone, desoxycorticosterone

acetate and occasionally insulin. Whatever oil vehicle was employed (and olive oil, sesame oil and coconut oil have been tried in an attempt to exclude carrier reaction) that oil was tested also as a control. So was cholesterol, the so-called mother substance of the steroids.

The test requires that 0.1 c.c. of the oil preparation containing 0.1 mg. of the hormone be introduced as a deep intradermal injection. The inner volar surface of the forearm, or outer upper arm, has been found most suitable.^{1,2} As a certain amount of the oil tends to run out of the puncture wound, however small, 0.12 c.c. is taken up by us. Separate tuberculin syringes and needles are used for each preparation. As protection against the small risk of oil embolism the plunger should be first withdrawn after introduction of the needle. The needle must be firmly held to the syringe to avoid leakage under pressure.

As reactions may appear weeks after injection, a standard site plan must be made and kept. The injections should be placed 1.5 inches apart. It has been our practice to use the code word OCOPOT down the length of the arm (olive oil control, cholesterol in oil control, oestrone, progesterone, oestradiol, testosterone) and to add to this basic code any other steroid hormones which may be available.

While accepting the standard of Zondek for a positive reaction (a red or rose-coloured papule, at least 0.5 cm. in diameter, or a pink zone of erythema 2.3 cm. in diameter) we regarded all reactions occurring up to 6 hours after injection as traumatic, and any (even within the qualifications of Zondek) which did not itch as 'questionable'. In all cases the patient reported back at 24 hours and 48 hours, and was asked to report any reaction in the injection site up to one month.

All cases giving a positive reaction to the controls were excluded from the series.

No cases were tested during their menstrual flow. A few who unexpectedly produced a period immediately after the injection did not appear to have their reactions affected. As reliance was placed on the retarded skin reaction, no specific time, relative to the period, was used for the tests.

There are two disturbing elements in the skin tests which we cannot explain. In the first, a patient originally clearly sensitive to oestrone (for example) and treated with improvement, may present herself months or years later with recurrence of the same symptoms. On this occasion the oestrone test will be nega-

tive, but progesterone and testosterone positive. She usually responds as well as previously to desensitization by the new allergen.

In the second, a patient sensitive to more than one hormone may respond to treatment with the combined preparation as successfully as the patient with a single sensitivity.

It is this type of apparently inexplicable result which has caused Baer *et al.*¹² to state: 'Tests for hypersensitivity to steroid hormones are, in our opinion, not suitable for routine diagnostic use.'

In the particularly sensitive patients of our series, as in that of Zondek's, the general symptoms of allergic response were precipitated by the test dosage. A common statement was: 'I feel as though I have all my symptoms back again.' This, with a positive skin test, was accepted as indicating a high degree of sensitivity to the endocrine. Urticaria occurred in one, but the severer symptoms of pyrexia, vomiting and shock were fortunately not met with.

For a very full and good review of the skin sensitivity aspect of the problem of endocrine allergy, readers are referred to the article by Pepys.¹¹

To me as a clinician, the most interesting skin tests have been the unusual ones, the retarded and the recurrent sensitivity reactions, but especially the former.

1. *The Retarded Periodic Skin Reaction.* This is a reaction in which an injection site, apparently negative and returned to normal, flares, one or two months, or each month later, with marked erythema and itching.

This reaction very frequently corresponds to the patient's expected time for the allergic symptoms of which she complains. We found, as did Zondek, that this critical phase occurred almost always in the premenstrual phase. Sensitivity to oestrone was most common.

We had two cases of recurrent stomal ulcers, occurring on the first and second days after the period, who produced marked reddening and urticaria on the day they had come to recognize as that of the monthly beginning of their distress. The appearance of a positive reaction on this day, after weeks without signs, was most dramatic. It is probable that at this time the relative reactive hormone levels are at their critical level, although not necessarily at their height.

It has been suggested that the retarded test reaction is in actual fact due to the slow decomposition of the oil in the skin and is a reaction to the vehicle itself. We, as others,

have tried various different oils and have not noted any great differences in the reactions. We have, however, had cases where there have been repeated cycles of complete inactivity between erythema and itching. We cannot see this as a reaction to anything but the hormone.

The reaction has been important in establishing our belief in this form of allergy.

2. *The Recurrent Test Reaction.* On occasions where the skin reactions have been negative we have felt that the investigation for an endocrine allergy has failed. Subsequently, when in treatment a large dose of the hormone has been given, the previously normal test site has flared up in a severe sensitivity reaction.

This happened in only two of our cases, but its importance is high in the general conception of allergy.

TREATMENT

In their first series Zondek and Bromberg treated 44 patients by desensitization. In 22 all symptoms disappeared, in 13 there was marked improvement and in 9 there was no amelioration.

Baer¹² treated two cases with hyposensitization, with very marked clinical improvement.

Wolf *et al.*⁶ reported 26 patients treated by desensitization. Complete relief was obtained by 6, and partial by 4 patients. Eleven patients were not helped, and 5 could not be followed.

Solari²⁰ reported several cases successfully treated including one of persistent pyrexia of 8 years' duration. He also reported a study of 52 patients, 22 of whom were treated with success.

Heckel⁵ had an over-all 84% success in subcutaneous hyposensitization with pregnandiol.

In our series 83 patients were treated by desensitization with the appropriate hormone, 81 women and 2 men; 40% have had complete relief from treatment (one course or more); 25% partial, and 35% were unaffected.

METHODS OF DESENSITIZATION

The methods of desensitization described by Zondek depend on the principle of protecting the affected organ by provision of small amounts of free circulating antibodies. He used three different methods, and these with modifications have been used by us.

1. All our patients were treated by subcutaneous injections.
2. Two slowly improving patients were given hormone peller implants.

3. Two cases of acne were finally treated by percutaneous inunction.

A fourth method has also been described for menopausal patients. In this a large dose of another hormone, e.g. testosterone in an oestrogen-sensitive patient, is given in an attempt to produce hypophyseal inhibition. This method was employed in 5 of our series. It was used by Zondek as a complete individual treatment. We used it to 'fix' the already encouraging result of percutaneous desensitization. In this it worked well. Because of the possible dangers, it was not used in the younger age group.

There is however at least one of my colleagues (Dr. J. Watson) who feels that the best clinical results are to be obtained by a short desensitizing course terminated by 3 injections of massive dosage. He finds that there is little difference whether this is the same hormone as that used for desensitization, or/and an apparently opposing one.

Technique of Percutaneous Desensitization. As this is the most common and useful form of treatment it will be given in detail.

The course is started with the smallest dose which produced a positive cutaneous reaction.

This, in our experience, has never been of a strength less than 0.01 mg. of the hormone in 1 c.c. of oil. The ordinary commercial preparations as put up for more massive therapy are perfectly suitable—there is no need for the pure crystalline hormone, as there is in the test preparations. We have used sesame oil as a diluting agent. Three concentrations of the hormone in oil are prepared: 0.01 mg. per c.c., 0.1 mg. per c.c. and 1 mg. per c.c.

Injections are begun with 0.1 c.c. of one of these preparations and are given daily. The dosage is gradually stepped up to a dose of 1 mg., or 24 injections, whichever may be reached first. We felt that nothing is to be gained by insisting on the longer course of 30 injections given by Zondek. Indeed, much 'patient resistance' may be built up.

The dosage should be held to low levels, or reduced if a general reaction occurs. The most usual untoward reaction is a severe local redness, itching and swelling in the area of the injection. The dosage should be adjusted to keep this reaction at a minimum. It is, however, desirable in our experience to produce some degree of local reaction. Patients state that they 'feel the effect more' when local redness and itching is present. In some patients this reaction may be produced by very small amounts, and it has been noted even following

injection by a grossly diluted preparation of 0.001 mg. per c.c.

The results obtained by the lower levels of dosage in particularly sensitive individuals produced a cure rate at least as good as when the maximal dose of 1 mg. was given. Nothing was lost by allowing the patients a holiday over week-ends.

Repeated Courses. In our experience symptoms tended to recur 6 months after the first course, when they were again controlled by a second course of 10 injections, starting from one fifth of the dose given as a final injection in the previous course.

A third course occasionally had to be given 9-12 months later. The relief of symptoms could then be regarded as 'permanent'.

In our more severe cases, where the first and second course gave definite but short-lived relief, we had good results, lasting over years, by the implantation of pellets of the same hormone.

It is important that one must not become bemused by therapy but always be prepared to review the difficult case. We have, for example, had a patient with headaches who improved, but not significantly, after her first course of desensitization. It was only at the end of the second course that she explained the other factor in her monthly headaches. Her husband was a commercial traveller and showed great resentment when his short period of return to the marriage bed corresponded with his wife's menstrual period. This etiology we felt was beyond the scope of our therapy.

There appears to be no necessity to stop treatment during a period, but the interval may be lengthened, e.g. every third instead of every second day. The menstrual flow has never been found to be definitely affected.

Where indicated by the skin tests, we gave a desensitizing course of two hormones at the same time and got some of our best results. From this one can only conclude that endocrine allergy is not a 'pure' allergy, as pollen allergy may be. One returns again to the search for the background allergen or the explanation of the role of the hormones as 'trigger' substances.

Implantation of Hormone Pellets. Pellets containing 15-25 mg. of the hormone to which the patient is sensitive were implanted subcutaneously in 5 patients. Where sensitivity to two hormones, e.g. oestrone and progesterone, was present, both steroid hormones were implanted. A cure or relief over two years was affected in 3 cases.

Percutaneous Desensitization. Desensitization by inunction of the commercial preparations of oestrone, progesterone or testosterone in lanolin, was not successful in our hands, even with acne, where the principal use would be expected to lie. All cases (6) after relative failure, were treated by injection. It is possible that continued treatment by inunction over months might be successful, but few patients can be found with the hardihood to continue with a type of treatment giving little early result. It is of passing interest that we have used inunction of histamine into the nuchal muscles at the completion of a histamine desensitization course in 9 patients. Six of the 9 have then passed from the 'uncertain' class to the 'quite well'.

Migrainous Type of Headache. Although we have treated more of this type of patient than any other, they have left in my mind the greater uncertainty. On analysis we do not think that this is because the concept of headache of a migrainous type arising from endocrine allergy is wrong (indeed, we are fully satisfied that it does exist, and that it responds to desensitization) but because we are satisfied that *all* headaches have more than one cause.

The majority (64%) of our patients have improved on treatment. These patients have had sufficient belief in the treatment to request further courses of injections on recurrence of pain. But the doctor is left with the uneasy assessment as to how far neurasthenic headache, nuchal spasm, alimentary and smoking indiscretions and lack of sleep, have been relieved by a belief, backed by some actual help.

Recurrent Ulcers in the Mouth. This category has been at the same time the most difficult and the most rewarding. There are not many women who suffer from distressing aphthous ulcers at, or about the time of the period, but such as there are, pass unsuccessfully from doctor to doctor, so that they become well-known. There are a few men also who exhibit a cyclical outbreak of painful mouth ulcers.

We have treated 8 women and 2 men. All had been extensively investigated by others or by ourselves for local, alimentary or haematogenous causes of ulcers. Three of the women were sensitive to oestrone and oestradiol, 3 to progesterone and 2 to both progesterone and testosterone; one man was sensitive to testosterone and one to oestrone.

Desensitization was carried out in all, with

relief of varying degrees. One woman (our first case) obtained freedom for 6 months from her first course, 9 from the second and has had no recurrence over 4 years since the third course. In her case we held to low dosage throughout.

A second patient, treated on a higher dosage schedule, got far worse attacks under treatment than she had had previously. These were eased by cortisone over the acute phase. On the completion of a second course in half dosage she obtained freedom for 4 months, after which contact was lost.

Our first male patient (after 6 years of exhausting ulceration) obtained freedom for 2 years following one course of oestrone, to which he was sensitive. The ulcers then returned. His sensitivity was re-checked and was again positive for oestrone. A further course was given. There has been no recurrence in the 4 years since then.

The second male patient was sensitive to testosterone. Ulcers tended to recur during

the course of hyposensitization, but wholly disappeared (for the first time for 2 years) 2 months later. He has now been free of ulcers for 3 years.

COMPARISON OF RESULTS

We have set our results in Table 1 to compare them with those of Zondek. We have not attempted to estimate the finer degrees of improvement, as these are too dependent on the view of the patient, except, e.g. in stomal ulcers and hydrarthrosis. The view of a patient whom one watches over the years, may vary from the first flush of enthusiasm: 'Doctor, I'm cured', to that 5 years later: 'But you know, I still get my attacks'. Although this is improvement, one cannot assess its degree.

DISCUSSION

The problems which others have noted in this fascinating subject of endocrine allergy have troubled us in our series. We have found the same difficulty in explaining the results of skin sensitivity—the occasional multiple response, the retarded reaction, the alteration of sensitivities in repeated tests. We have been puzzled by the irregularity of response to desensitization, the appearance of a different allergic symptom and new hormone sensitivity after a treatment course, and the apparent inconsequential result of terminal massive dose therapy. At the same time we have noted, as others have before us, an improvement or cure of symptoms in more than 60% of patients treated by this means. These observations together make an intriguing, ill-disciplined and frustrating combination. Many factors have still to be evaluated.

It may be that there is no independent hormone. It may be that the essential substance has not yet been discovered. Heckel has suggested that this substance is pregnandiol and has produced a series of impressive results in premenstrual distress, ovarian pain syndrome, painful breasts, endometriosis, menorrhagia, generalized pruritus or pruritus vulvae and ani, and various disorders related to the menopause, which he has treated by desensitization with this substance. This success has been accredited by certain allergists to the fact that pregnandiol 'is a cocktail of hormones'.

Another colleague²¹ is getting impressive results with chorionic gonadotrophin. He is using the commercial and not the pure preparation for this tests.

The proposition has been advanced that the final explanation will rest on a Selye adapta-

TABLE 1:
COMPARISON OF RESULTS OF TREATMENT
(Z = Cases treated by Zondek;
C = Cases treated by present author).

Diseases Treated		Number of Cases Treated	Recovery	Improvement	No Result
Asthma	Z	3	1	2	—
	C	10	3	4	3
Vasomotor Rhinitis	Z	2	1	1	—
	C	4	2	2	—
Angioneurotic Oedema	Z	2	2	—	—
	C	—	—	—	—
Chronic Urticaria	Z	4	2	2	—
	C	4	3	1	—
Chronic Eczema	Z	1	—	—	1
	C	—	—	—	—
Acne	Z	3	—	2	1
	C	6	—	2	4
Migraine	Z	8	4	2	2
	C	40	17	8	15
Superficial Keratitis	Z	2	2	—	—
	C	1	1	—	—
Recurrent Conjunctivitis	Z	2	—	2	—
	C	2	—	2	—
Premenstrual Tension	Z	12	7	2	3
	C	—	—	—	—
Pruritus Vulvae	Z	10	5	2	3
	C	3	—	2	1
Menorrhagia	Z	—	—	—	—
	C	2	—	2	—
Premenstrual Fever	Z	2	2	—	—
	C	—	—	—	—
Stomal Ulcers	Z	—	—	—	—
	C	10	4	3	3
Intermittent Hydrarthrosis	Z	—	—	—	—
	C	1	1	1	1

tion where the inter-relationship of pituitary, adrenals and ovary is disturbed on its axis, and allergic and non-allergic states are subsequently produced.¹⁷⁻¹⁹

Randolph has stated that allergens arise within the body as products of diseased or functionally altered organs. Zondek and Bromberg do not suggest that the endocrine glands are 'diseased or altered'. From our own observations it would appear that the allergy has risen as a result of mildly altered glandular function and we quote in support of this the improved libido in several cases, following a course of therapy (although this may be due as much to improved health as actual readjustment of endocrine balance) and 4 pregnancies following on treatment where 3-7 years of marriage had been barren.

To all these problems must be added the 'imponderables', the psychogenic elements present in all allergic diseases.

SUMMARY

The concept of endocrine allergy provides a cure or amelioration for 50% to 60% of patients sensitive to their own hormones, for whom no real hope could otherwise be offered.

It provides a method of investigating the otherwise obscure forms of menstrual, puberty, pregnancy or menopausal allergy. These cases are not common, but their distress is considerable and frequently widely known.

It is evidently not a 'pure' allergy. Investigation and treatment are complicated by the 'switches' in the hormonal pattern, and by the fickleness of the 'crucial' phase.

It is a subject on which it is unwise to theorize. It is interesting that even the greatest authorities have plunged once or twice and not again; but it is a subject clinically rewarding and, experimentally, almost untouched.

OPSOMMING

Die begrip van endokrienallergie bied genesing of verligting aan 50% tot 60% van die pasiënte wat gevoelig vir hul eie hormone is, en vir wie daar andersins geen werklike hoop bestaan nie.

NOTES AND NEWS • BERIGTE

'MEDICARE' IN MASSACHUSETTS

The nineteen-page outline of procedures for implementing the Dependent's Medical Care Act (Public Law 569—84th Congress, popularly termed 'Medicare'), distributed recently with various enclosures to physicians in Massachusetts by the Massachusetts Medical Service in its role of fiscal administrator of the law for the Massachusetts

Dit bied 'n metode vir die ondersoek van andersins obskure vorms van menstruasië-, puberteits-, swangerskap- of menopouse-allergie. Hierdie gevalle kom nie dikwels voor nie, maar hulle kan aansienlike ellende veroorsaak en is dikwels goed bekend.

Dit is klaarblyklik nie 'n suiwer' allergie nie. Ondersoek en behandeling word bemoeilik deur die 'veranderings' in die hormoonpatroon, en deur die onbestendigheid van die 'kritieke' fase.

Dit is 'n onderwerp waarvoor dit nie raadsaam is om bespiegeling te maak nie. Dit is interessant om daarop te let dat selfs die grootste gesaghebendes een of twee keer 'n kans gewaag het, maar nie weer nie; maar dit is 'n onderwerp wat klinies belonend en eksperimenteel byna onaangeraak is.

I wish to thank Saphar Laboratories, Ltd. and Scherag (Proprietary) Ltd., who made available pure hormones for test purposes; and all the doctors—especially of our team at Vanderbijl Park—who allowed me to investigate their cases.

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Medical Society, is the culmination of a series of conferences by the Society's agents to effect a programme suited to the area and its medical practitioners.

As in the administration of any governmental programme requiring the expenditure of public funds, 'Medicare' will necessitate the study by participating physicians of a series of regulations and stipulated allowances and the filling out of forms.

Admittedly, paper work is always a problem. There are physicians who can take such burdens in their stride. There are others who may understandably never become accustomed to the paper work now becoming a permanent procedure in medical practice.

There may be questions concerning the schedule of fees for medical and surgical services, the latter schedule covering approximately 1,500 procedures, and in general being at the Blue Shield Plan B level.

The 'Medicare' plan became effective on 7 December 1956. That wrinkles will develop goes without saying. These wrinkles will be ironed out as the programme progresses.

The basic philosophy of the programme—providing the wives, dependent husbands and children of the uniformed services with medical care from civilian sources—is one to which all can subscribe.

That such legislation was passed in an era that is seeing an ever-increasing federal encroachment on the private practice of medicine is a tribute to organized medicine that supported the passage of Public Law 569.

The introduction to the aforementioned manual of procedures distributed by the Massachusetts Medical Society's fiscal agent concludes as follows:

The active interest and co-operation of privately practising physicians throughout the United States and its territories in organizing their efforts to provide their services in the discharge of the Government's responsibility to its defenders, is living testimony of the integrity and responsibility of the medical profession in maintaining the American way of life under a free enterprise system.

The responsibility for the success of 'Medicare' rests now with the practising physician.

[From *The New England Journal of Medicine* (1957): 256, 89.]

THE RHEUMATISM ASSOCIATION OF SOUTHERN AFRICA

On 12 October 1956, Prof. R. M. Stecher of the School of Medicine, Western Reserve University, Cleveland, Ohio, and President, *Ligue Internationale contre le Rhumatisme*, addressed a meeting of medical practitioners in Johannesburg. As a result of the stimulus provided by his address, the principle of establishing a Rheumatism Association of Southern Africa was accepted, and a Steering Committee was appointed to prepare for the establishment of such an Association.

On 25 February the Steering Committee reported back with a Constitution for the proposed Association. This Constitution, after some minor amendments, was adopted. Its objects include the following:

1. The study and promotion of knowledge of the rheumatic and allied diseases.
2. The stimulation and co-ordination of research in the field of the rheumatic and allied diseases.
3. The promotion of measures, and the organization of programmes of treatment, designed to alleviate suffering from the rheumatic and allied diseases.
4. The promotion of the establishment of special clinics or centres for patients suffering from the rheumatic and allied diseases.

5. The promotion of procedures designed for the rehabilitation of those suffering from the crippling effects of the rheumatic and allied diseases.

6. The establishment of Branches of this Association in the Southern portion of the African continent.

The In augural Meeting of the new Association was held at 8 p.m. on Wednesday, 3 April 1957, at Medical House, Esselen Street, Johannesburg. Those interested in obtaining further details should communicate either with Dr. E. B. Woolf, 34 Jan Smuts Avenue, Forest Town, Johannesburg (telephone: 41-2457) or Dr. A. L. Lomey, 509 Medical Centre, Jeppe Street, Johannesburg (telephone: 22-2052).

It is also anticipated that a large meeting of the Rheumatism Association will be held at the time of the Medical Congress in Durban during September 1957.



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Dr. G. P. Charlewood, of Johannesburg, left at the end of March on a Bernhard Baron Travelling Scholarship for a 2-month tour of Nigeria, Ghana, Belgian Congo, Uganda, Tanganyika and the Central African Federation.

The purpose of Dr. Charlewood's trip is to make a special study of Bantu gynaecology.

BLOOD GROUP CHARTS

Dade Reagents, Inc., of 1851 Delaware Parkway, Miami 35, Florida, U.S.A., have recently issued 2 new charts—'Rh-Hr Phenotypes and Genotypes' and 'Blood Groups'.

These concise summaries constitute valuable reference charts for all those interested in blood groups.

Medical practitioners wishing to obtain copies of these charts should address their requests direct to Dade Reagents, Inc.

Dr. J. Tertius Rossouw of Johannesburg, will attend the Sixth International Congress of Otolaryngology to be held in Washington from 5-10 May 1957.

During his trip overseas Dr. Rossouw will be visiting various leading clinics in South and North America, as well as in Germany. He expects to return to the Union by the end of October 1957.

TRANQUILLIZERS

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SEAMUS FLEMING.

From the *New Yorker*, 1 September 1956, p. 77.

REVIEWS OF BOOKS

HANDBOOK ON FLUID BALANCE

Fluid Balance Handbook for Practitioners. By William D. Snively, Jr., M.D. and Michael J. Sweeney, M.D. 1956. (Pp. 309 + Index. Illustrated. 51s.) Oxford: Blackwell Scientific Publications.

A thorough knowledge of fluid and electrolyte balance is essential for the adequate care of the sick. In this monograph the authors have attempted to combine the fundamental, accepted facts with an essentially practical approach. The first part deals with 'foundation facts'. Succinct descriptions of the body fluids serve to introduce the second part—clinical diagnosis. Three basic types of specific fluid imbalance are described. The first type includes changes in the properties of the extra-cellular fluid. This type includes volume changes, electrolyte concentration changes and electrolyte composition changes.

The second basic type embraces those due to the position of extra-cellular fluid, characterized by a shift of water and electrolytes from plasma to interstitial fluid and vice versa.

The third basic type includes changes in the nutritional status of the body as a whole. Clinical features of the various states are described and limitation of laboratory control indicated.

Therapy is discussed in Parts III-V. The average daily requirements are calculated per unit of body surface. The balanced solutions used orally and intravenously are those advised by Butler and Talbot, Lowe, and Darrow and Cooke. Replacement solutions are calculated to meet current maintenance needs, correct deficits, and replace concurrent losses. The rate of administration is also calculated on a unit per square metre of body surface. Due regard is given to the importance of impairment of homeostasis in the treatment of patients. The handling of certain excesses, e.g. extra-cellular fluid volume, potassium and calcium is detailed. Fluid shifts between plasma and interstitial fluid are associated with the maintenance of blood pressure and remobilization of oedema fluid. Nutritional status changes include the handling of protein, caloric and vitamin deficits. Part VI discusses the routes of administration—the parenteral route is the most efficacious.

'Down to cases' forms the basis of Part VII. Clinical problems are analysed and the management in picked examples is explained on the basis of the previously enunciated principles. The last chapter is devoted to the 'workshop' exercises for those who feel they are now capable of handling fluid and electrolyte balance in the sick.

The book is well written and each chapter commenced with an appropriate quotation. A large

number of figures and Tables helps to explain many of the difficulties associated with the problems of fluid and electrolyte balance. This book well deserves a place on the shelf of practising doctors who are confronted with the handling of this most important aspect of the ill patient.

TUBERCULOSIS

Symposium of Tuberculosis. Edited by F. R. G. Heaf, M.A., M.D., F.R.C.P. 1957. (Pp. 721 + Index. Illustrated. Five guineas.) London: Cassell & Company Limited.

This *Symposium of Tuberculosis* has been compiled by many eminent authors, for the use of undergraduate and post-graduate students. The treatment of the disease is discussed from all aspects, special consideration being given to the fact that in some countries surgical facilities are limited, and older methods must remain the basis of treatment.

A large section of the book has been devoted to the study of non-respiratory tuberculosis which, although it falls under the surveillance of the orthopaedic surgeon, yet remains a subject of great importance to every chest physician.

The introductory chapter describes some of the generally accepted and better known facts about the disease, in order that the reader can clearly understand the rationale underlying the tuberculosis services. Emphasis is laid on the greatly improved outlook for recovery for these patients.

The results of BCG vaccination are reviewed, and the inconclusive conclusions may best be demonstrated by quoting:

'After thirty years' experience, during which millions have been vaccinated against tuberculosis, it can be said that the results indicate that BCG confers some protection against primary tuberculous infection.' . . . 'The vaccine is a variable preparation, and its effect on different individuals is by no means constant.' . . . 'Opinions differ as to whether it is better to create a tuberculin positive population or a tuberculin negative one.' . . . 'The position of BCG is still not at all clear.'

It is stated in the chapter on infection and immunity that tuberculous pleurisy with effusion occurs more commonly as a complication of the primary lesion in adolescents rather than in young children. Primary tuberculosis is seen more frequently to-day in young adults, as an increasing proportion of children reach the susceptible stage of life without having been previously infected. An examination of the mortality rate shows that the mortality is falling, but this would be more impressive if it were accompanied by a decrease in the numbers of new cases.

The chapter dealing with treatment discusses the different methods at length and it is stated that, generally, the more extensive the disease and the more ill the patient, the less desirable is domiciliary treatment. Patients can never be too ill, therefore, to be admitted to hospital.

A careful description is given of all the public health measures and the types of record-keeping which should be an adjunct to any thorough and proper programme.

The several chapters on the non-respiratory forms of tuberculosis stress again the value of antibiotic treatment. Tuberculosis in children, tuberculosis in the tropics and the effect of tuberculosis on industry all prove interesting subjects for discussion.

The authors state that in a work covering so wide a field it has not been possible to eliminate conflicting opinion. In fact, the very difference of opinion of the various authors regarding the pathogenesis and treatment of the disease makes it stimulating reading.

The combination of excellent presentation with clear and well-chosen contributions makes this symposium of importance to any student of any aspect of tuberculosis.

ANATOMICAL TECHNIQUES

Anatomical Techniques. By D. H. Tompsett, B.Sc., Ph.D. 1956. (Pp. 237 + Index. With 83 Figs. 35s.). Edinburgh and London: E. & S. Livingstone Ltd.

There are now 5 Medical Schools in South Africa, each with its Department of Anatomy. One of the problems in all 5 Schools is the increasing difficulty in obtaining material for dissection. For this reason alone it has become urgently necessary to preserve such material as becomes available in a museum. Furthermore, each prepared specimen must be used to the best possible advantage, lest the opportunity to replace it with a better one is not soon forthcoming.

Dr. Tomsett's book *Anatomical Techniques* provides the Museum Curator and the occasional dissector with precise and lucid details of the most modern techniques for preparing and preserving specimens for display under cover. The techniques embrace methods of fixation, injection of coloured substances, mounting in transparent containers, illustration, casting vessels, ducts and cavities (of the brain, labyrinth, heart, lungs, liver and kidneys), embedding of specimens in transparent blocks, modelling in wax and resin and staining of brain slices.

There are however several omissions which are unexpected in view of the title. The emphasis is on perspex and resin techniques, to the exclusion of other important methods. The notable omissions are the preparation, protection and storage of wet specimens, permitting free handling, the mounting of serial sections, including transparent whole organ slices (which help to bridge the gap between gross anatomy and histology), the preparation of skeletons and single bones, the mounting of articulated bones to show movements at a joint, the reconstruction of soft tissues on bony frameworks, the preparation of adult and embryological models in plaster and papier mâché, and the casting of face masks and accurate reproductions of original specimens.

With the inclusion of these methods, which are

probably well within the scope of the author, the book will undoubtedly become a standard treatise.

CHRISTOPHER'S SURGERY

Christopher's Textbook of Surgery. Edited by Loyal Davis, M.D. 1956. 6th ed. (Pp. 1484. With 1359 Illustrations. \$15.50). Philadelphia and London: W. B. Saunders Company.

This authoritative textbook has now reached its sixth edition. The new volume has been necessary to keep up with the rapid progress that surgery is making. The author, Dr. Loyal Davis, invited 87 contributors to cover each section and a list of the contributors reads like a 'Who's-Who' of American surgery. Surgeons such as Whipple, Churchill, Hufnagel, Walters, Marshall and Blakemore, and others too numerous to mention, have become household names to most doctors.

Chapters on fluid balance and endocrinology have been added and are easily understood. The new conception of milli-equivalents and acid-base replacement is explained simply. The chapter on antibiotics and chemotherapy includes all the modern broad-spectrum antibiotics. There is also a detailed modern treatment for tetanus.

Thoracic surgery is fully dealt with and the chapter on cardiac surgery by Hufnagel is a classic. It familiarizes not only medical students but also post-graduates on what is being achieved in cardiac surgery.

The chapter on pancreatic surgery is full and detailed and the treatment of acute and chronic pancreatitis is discussed. In the section on the gall bladder and bile ducts, early operation for acute cholecystitis is advocated, without a discussion of the dangers. In a textbook of this nature, the conservative treatment should be given more prominence.

Modern branches of surgery, e.g. the surgery of the vascular system, are included and the technique of arterial grafting is given.

The diagnosis, treatment and prognosis of fractures and bone pathology is noteworthy for its clarity and the excellence of its illustrations. Copeland and Geschicter stress the poor prognosis of bone sarcoma and mention the use of deep X-ray therapy in attempting to treat these tumours. They feel that it may be used as a pre-operative measure but do not hold out much hope for it.

It is pleasing to see a whole chapter on the hand, both injuries and infections of which are included. Primary suture of tendons and nerves is advocated in clean wounds. The present British tendency of delayed suturing and tendon grafting is not considered.

The chapter on the thyroid gland is somewhat dogmatic and only gives the views of the Cleveland Clinic. The genito-urinary section of the book is relatively sketchy compared with the generally high standard in the rest of this book.

This textbook fulfils an excellent purpose and although it may be too detailed in some sections for the undergraduate student, it is an outstanding reference work. Its general text is sound and its teaching acceptable. It can also be used by post-graduate students for general reading in surgery. It is invaluable to the general practitioner who wishes to refer to and refresh his acquaintance with a surgical subject. At the end of every section is a full list of recent references for more detailed reading.



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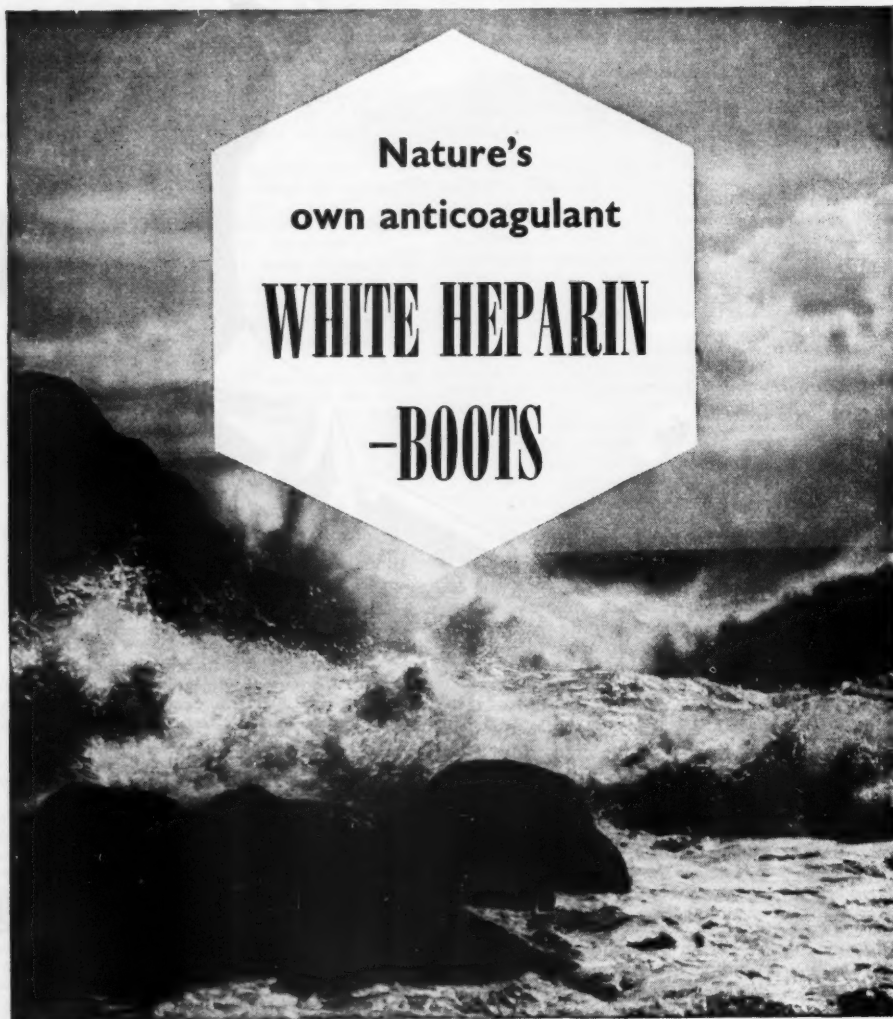


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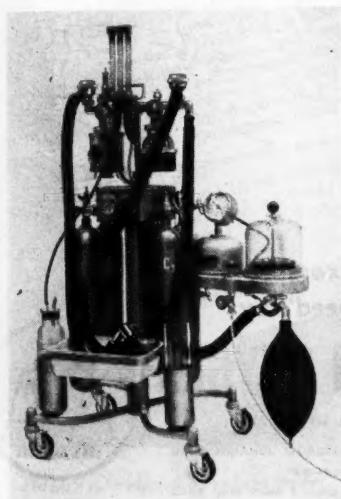
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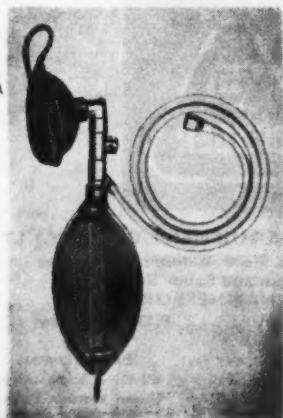
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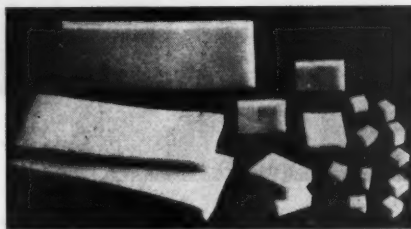
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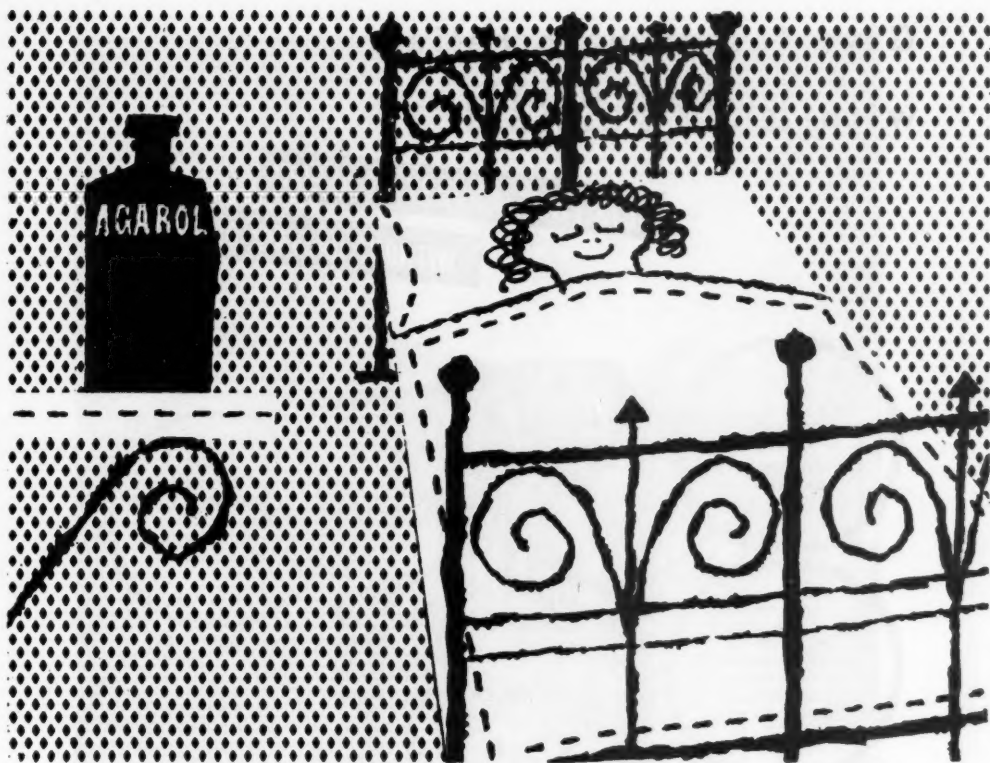
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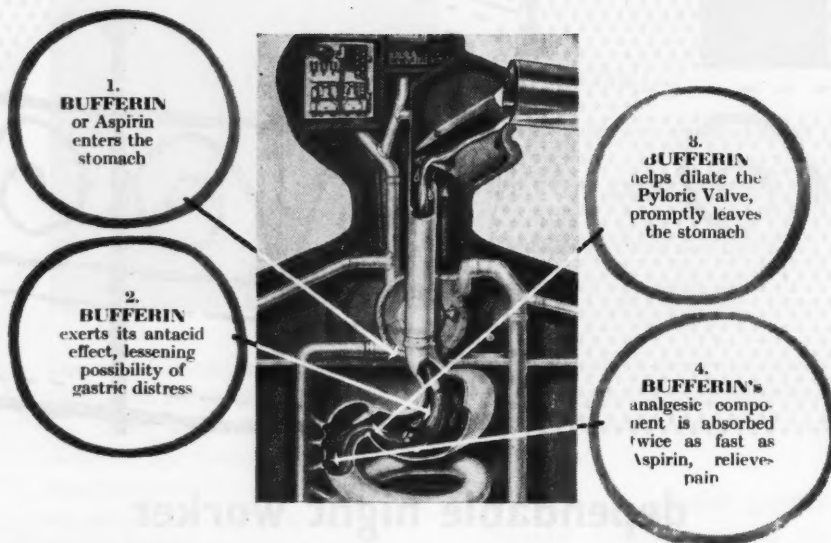
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